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OFFICIAL JOURNAL of the AMERICAN HEART ASSOCIATION

The George E. Brown Memorial Lecture

Digital Rheoplethysmography

By G. E. Burch, M.D.

IT is indeed a great honor to deliver this George Brown Lecture of the American Heart Association. I wish to express my appreciation to the Chairman, other officers, and members of the Section on Circulation for this opportunity. Dr. Brown was responsible in large part for organization of this Section, the oldest and most protean in its interests, covering all phases of science of the circulation regardless of discipline. I have selected to discuss recent studies in rheoplethysmography, firstly, in honor and memory of Dr. Brown, whose main interests were in the peripheral circulation, and, secondly, because the approach is new, the observations, applications and concepts are thought provoking, and, as in any new scientific approach, many problems remain to be solved.

The rate of blood flow to organs and local tissues has interested many investigators for many years. Although methods for measuring the rate of circulation of blood through organs and tissues have varied, the fundamental and standard approach has been that introduced by Brodie and Russell[1] and Hewlett and Van Zwaluwenburg.[2] These investigators showed that the rate of blood flow to a part, such as the hand, foot, or segment of a limb, or to an organ, such as the kidney, may be recorded by enclosing the part in a rigid plethysmographic chamber connected by rigid tubing to a flexible bellows, which activates a wooden or light lever to record movements on smoked or photographic paper (fig. 1). Any change in volume of the part displaces air or water within the plethysmographic chamber, which, in turn, displaces the flexible bellows an equal volume, and produces a deflection on the recording paper.

This principle of plethysmography has been in use in physiology for many years. These investigators[1, 2] showed that if venous outflow to the part enclosed in the plethysmographic chamber were suddenly obstructed by a pressure lower than the diastolic arterial blood pressure, the part would increase in volume due to inflowing blood. Since the moving paper records lapse in time and since the linear deflection produced by the recording lever is calibrated in volume change, a volume-time cartesian-type graph is automatically charted. From such a completed record it is possible to obtain the rate of volume change of the part or the rate of inflow of blood to the part (fig. 2). It has been customary to draw a straight line tangentially to the trace and to determine from its slope the mean rate of blood flow to the part. This method of venous occlusion for

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measuring blood flow to a part has been modified considerably during the past 50 years to satisfy various experimental requirements,[3-10] but all measurements have been limited to estimates of mean rate of inflow of blood to the part. It continues to serve physiologic purposes well and is still considered the procedure by which all other methods are standardized.

Unfortunately, this method has not received critical evaluation; its validity has been mainly inferred. No satisfactory method has yet been devised for its adequate evaluation under the conditions of animal research. In spite of these deficiencies, it can provide useful information concerning the peripheral circulation. Some of the problems inherent in the venous occlusive plethysmographic method have been discussed briefly elsewhere[11] and will not be reiterated here. The magnitude and significance of the problems must be known to the investigator for proper evaluation of his data. Some of the difficulties are evident in published data and reflect errors of variable significance. These and other problems have been considered in these rheoplethysmographic studies and many have been eliminated or controlled. Those that remain require continued attack if the rheoplethysmographic method is to become fully developed and accurate. The main source of difficulty is the volume artifact previously discussed.[11]

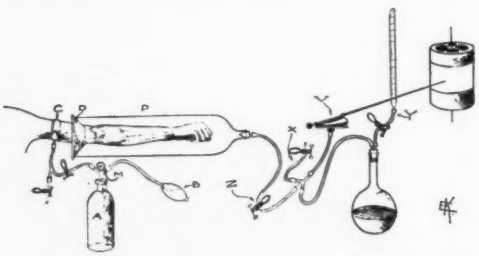

FIG. 1. Diagram of the venous occlusive plethysmographic method introduced by Hewlett and Van Zwaluwenburg for measuring the rate of blood flow to the arm of man. (From *Heart* **1**: 87, 1909).

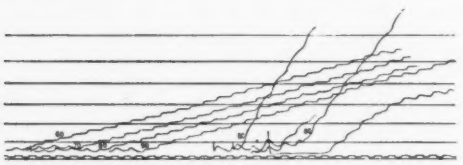

FIG. 2. A typical plethysmogram obtained by Hewlett and Van Zwaluwenburg. The mean slope of the curves was used to calculate the mean rate of inflow. (From *Heart* **1**: 87, 1909).

It is not the intention of this report to review historically the technic of venous occlusive plethysmography or to discuss its problems but merely to present the rheoplethysmographic method and to indicate some of its qualitative and quantitative potentialities for the study of the peripheral circulation. The present discussion is limited to the human digit, since the method has been developed and used primarily for the digits of intact man; with relatively simple modifications it can be applied to other organs.

THE RHEOPLETHYSMOGRAPH

A digital plethysmograph sensitive to a volume change of 0.1 mm.^{3} or less and with satisfactory physical characteristics to record volume change accurately has been developed.[11-17] Many of the problems of leakage, difficulties in usage, and other complications have been eliminated,[11, 14] and the recordings are now technically satisfactory. In addition, a simple electronic method has been designed to occlude digital venous outflow automatically at any preselected period in the pulse cycle for any preselected duration.[11] The rheoplethysmographic apparatus and method from the point of view of the instrument are satisfactory.[11]

THEORETIC CONCEPT

If a digit is enclosed in a lightweight, properly fitted plethysmographic cup (fig. 3) connected to a suitable plethysmograph and if obstruction to venous outflow is suddenly produced, the recording camera being set at a fairly rapid speed to reveal detailed changes, a plethysmogram (fig. 4) will be recorded that presents detailed information not obtainable from the conventional plethysmogram.[1-10]

As indicated previously,[11] the pressure in the occluding cuff obstructing venous outflow should not interfere with inflow, but, unfortunately, it does to a slight, although probably negligible, extent.[11] Venous occlusion is produced by inflation of a flexible rubber digital

occluding cuff to a pressure of 60 mm. of Hg. Preferably, the occluding pressure should be varied to meet the specific needs of the circulation at the moment of occlusion, but in these experiments a pressure of 60 mm. was used except as indicated.[11] With the subject resting quietly in a hospital-type bed in the comfortable atmosphere of a specially designed room[11, 14] and with the digits resting at heart level on an arm rest, venous outflow in 2RF was suddenly occluded. The completed rheoplethysmogram (RPG), as shown in figure 4, reveals simultaneous recordings for the second right fingertip (2RF) and third right fingertip (3RF). The sudden rise in the volume trace for 2RF (fig. 4) was produced by two factors: (1) accumulation of inflowing blood (I_V) within the digit enclosed in the plethysmographic cup and (2) an artifact (A_V). Since the traces for 3RF and 2RF were simultaneously recorded,

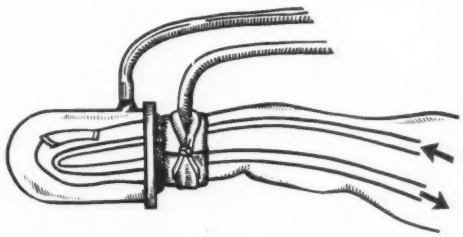

FIG. 3. The plastic, transparent, and lightweight plethysmographic cup and the venous occlusive, or collecting, cuff are shown mounted on the terminal portion of the index finger. The finger or toe tip is defined as that portion of the digit distal to a plane in which lie the major dorsal and palmar or plantar creases in the region of the distal interphalangeal articulation. The digital circulation is diagrammatically shown. When the venous occlusive cuff is suddenly inflated to a pressure less than diastolic arterial blood pressure, inflowing blood is trapped distal to the occluded digital veins within the vessels of that portion of the digit enclosed in the plethysmographic cup, in which the increase in volume of the part is recorded by the plethysmograph.

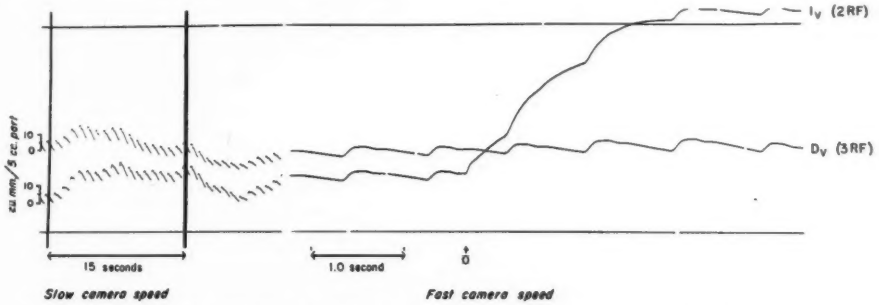

FIG. 4. A rheoplethysmogram showing the simultaneously recorded curves of the volume-time course for the second right fingertip (2RF) and the third right fingertip (3RF) of a normal subject resting in bed in a comfortable atmosphere with the digits at heart level. The recordings are shown at slow and fast camera speeds. The venous occlusive cuff was suddenly inflated to 60 mm. Hg pressure at the arrow 0. The resultant collection of blood in the vessels distal to the occluded digital veins caused 2 RF to increase in volume as indicated by the trace. This I_V curve actually includes the artifact curve, A_V (see figs. 5 and 6).

any volume change in 2RF can be readily timed in the pulse cycle.

The volume of inflow is obtained by subtracting the volume change produced by the volume artifact (A_V) from the recorded trace for 2RF. This is done by obtaining the curve of the volume-time course of the artifact under the same circumstances as those that existed when the inflow trace for 2RF was recorded. The volume-time course of the artifact is recorded in the following way. The circulation to the arm is arrested by sudden inflation of a blood pressure cuff applied to the brachium with a pressure well in excess of systolic arterial pressure. When the circulation in the digit becomes stabilized, the venous occlusive cuff on the digit is suddenly inflated to a pressure of 60 mm. Hg, and the volume-time course of the artifact (A_V) is recorded (fig. 5). This curve is then subtracted from the volume trace, as

FIG. 5. The artifact volume curve (A_V) was obtained by first arresting the circulation to the digits under study by inflation of a blood pressure cuff applied to the arm (brachium), followed by sudden inflation (at arrow 0) of the digital venous occlusive cuff to the same pressure and under the same experimental conditions as existed for the recording of digital blood flow in figure 4. The return of the A_V curve toward its former level occurred with sudden release of the pressure in the venous occlusive cuff.

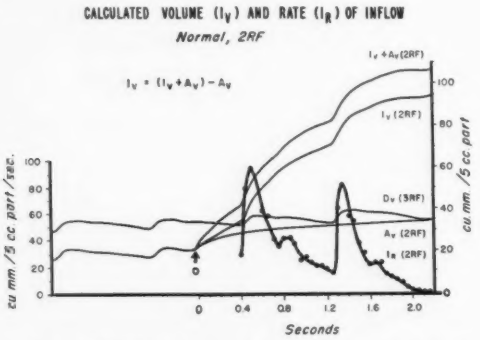

FIG. 6. Method for converting manually the recorded rheoplethysmographic curve of the volume-time course of 2RF, which contains I_V and A_V, to volume inflow (I_V) by subtracting from it the volume artifact curve, A_V. The curve of the recorded rate of inflow (I_R) is the first derivative of the I_V curve. The gradual decline in rate of inflow for the second pulse cycle is due to leakage past the venous occlusive cuff, to a decline in A-V pressure gradient produced by the blood collecting in the digital vessels, or to both these factors.

previously described,[11] the resultant curve representing the volume-time course of inflow (I_V) (fig. 6).

Obviously, the accuracy of the I_V curve depends upon the accuracy of the artifact curve, still a major problem in the method, discussed more fully elsewhere.[11] If the procedure is employed carefully, the artifact can be fairly accurately recorded and subtracted, especially if the first 0.20 second after application of the digital occluding pressure is disregarded and only the remainder of the trace is employed.

Since the volume pulse wave (fig. 7) is recorded simultaneously with the inflow trace (I_V) and represents the time course of the difference (D_V) between the volume of inflow (I_V) and volume of outflow (O_V), then:

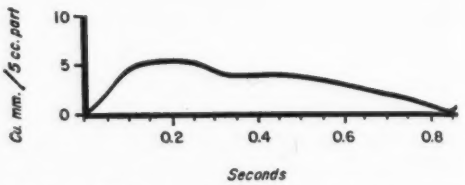

FIG. 7. This volume pulse wave is the same one shown in figure 6 for 2RF immediately prior to digital venous occlusion. This volume curve represents the time course of the difference (D_V) between volume of inflow (I_V) and volume of outflow (O_V). The pulse wave recorded simultaneously for 3RF, after correction for size of the digit, can be employed interchangeably in these analyses with the pulse wave recorded for 2RF.[12] The similarity of these pulse curves is evident from figure 6.

$$D_V = I_V - O_V . \qquad (1)$$

Since D_V and I_V are actually recorded, the time course of the volume of outflow (O_V) is obtained by subtracting D_V from I_V, or:

$$O_V = I_V - D_V . \qquad (2)$$

D_V is recorded for 3RF simultaneously with the time course of inflow (I_V) for 2RF. If it is assumed that D_V of 3RF, after correction for size of the digit, is the same as for 2RF, then D_V for 3RF may be subtracted from I_V for 2RF to obtain O_V for 2RF. Or, a suitable D_V trace recorded for 2RF for the pulse cycle immediately preceding occlusion to venous outflow may be used to obtain O_V for 2RF. No significant difference was observed in these two methods when they were properly used.[11] In these experiments the D_V curve for the same digit recorded just before venous occlusion was used to obtain the O_V curve for that digit. Thus, whereas in the strict sense the I_V, O_V, and D_V curves so obtained are not simultaneously recorded, they may be so considered under proper conditions. Three such volume curves are shown in figure 8. This venous occlusive plethysmographic method for obtaining continuous volume inflow and outflow curves for a single pulse cycle has been called *rheoplethysmography*.

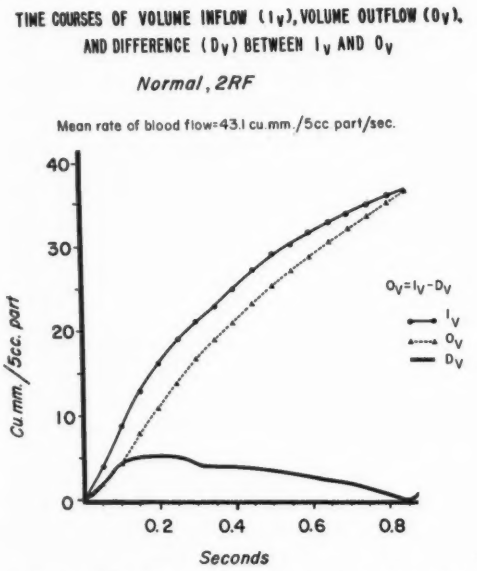

FIG. 8. The simultaneous inflow (I_V), outflow (O_V), and the difference (D_V) volume curves for a single pulse cycle. By reference to the simultaneously recorded volume pulse wave, it is possible to know the volume changes in inflow and outflow for any moment in the pulse cycle.

Since the volume curves (fig. 8) are continuous for a single pulse cycle, the first derivatives of the volume curves are simultaneous time courses of the rate of inflow (I_R), rate of outflow (O_R), and difference (D_R) between the rates of inflow and outflow (fig. 9). The curves of the time courses of acceleration (I_A, O_A, D_A) are the second derivatives of the volume curves (fig. 10). It is possible to plot indefinitely the successive derivatives of these curves, but beyond the second derivative they have only mathematic and no known physical or physiologic significance. The volume-time courses are moment-to-moment indices of *energy* associated with inflow, outflow and difference between inflow and outflow; the rate curves are moment-to-moment indices of *power* associated with these phenomena; and the acceleration curves are indices of *accelerations in power*. These physical aspects of the curves have received little attention.

These families of simultaneous curves lend themselves to various analyses of the peripheral circulation that were heretofore impossible. For example, since they are continuous throughout the pulse cycle and since the volume pulse wave (D_V) is recorded simultaneously, any phase of inflow or outflow may be related to any moment in the pulse cycle and, in turn, to the corresponding cardiac cycle. Furthermore, changes in inflow can be related to outflow and changes in outflow to inflow.

Since inflow occurs by way of the arteries supplying the part, the inflow curves reflect the behavior of the arterial side of the circulation, and since outflow occurs by way of the veins, the curves of outflow reflect the behavior of the venous side of the circulation. By integration of such principles with others in rheoplethysmography and plethysmography, these approaches can be extended much further to the understanding of the peripheral circulation. Some of these applications to normal and abnormal physiologic processes in the peripheral circulation are presented in this lecture

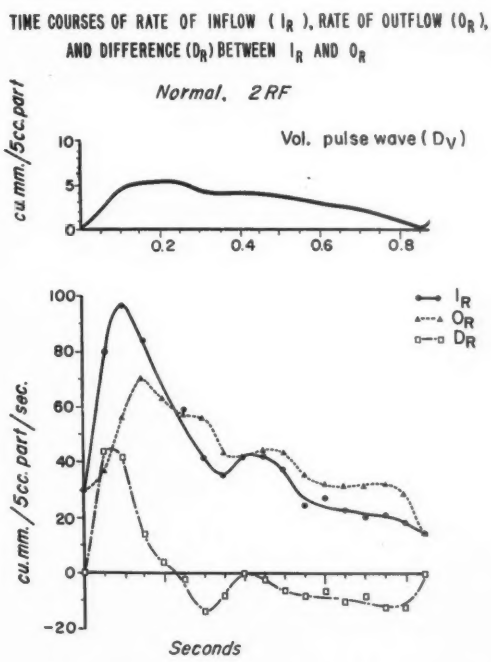

FIG. 9. The simultaneous curves of rate are the first derivatives of the volume curves shown in figure 8. Inspection of these curves reveals the rate of inflow and outflow and the difference between the rates of inflow and outflow for any moment in the pulse cycle.

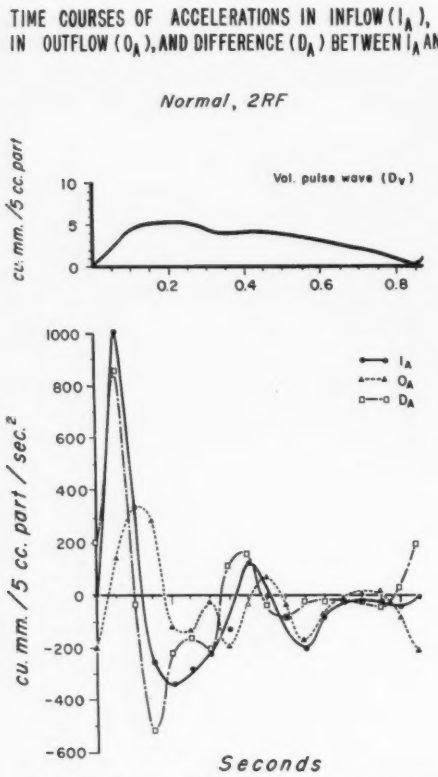

FIG. 10. The simultaneous curves of acceleration are the second derivatives of the volume curves shown in figure 8.

primarily to illustrate the potentialities of this method in the study of the intact circulation in an organ such as the digit rather than to define aspects of the circulation for any particular circulatory state.

In association with Mr. J. A. Cronvich, a new electric type of rheoplethysmograph (fig. 11) was developed[15] that makes it possible, by means of transducers,* suitable circuits, and a group of nine galvanometers,† to record simultaneously and automatically the rheoplethysmographic volume (R_V) and rate curves (R_R). A typical record is shown in figure 12. All rheoplethysmograms presented in this report were obtained with this recorder. Methods for obtaining the dimensions of the digits, standardizing the galvanometers, correcting for size of the digit and converting the data to proper units have been discussed in detail elsewhere.[11, 14]

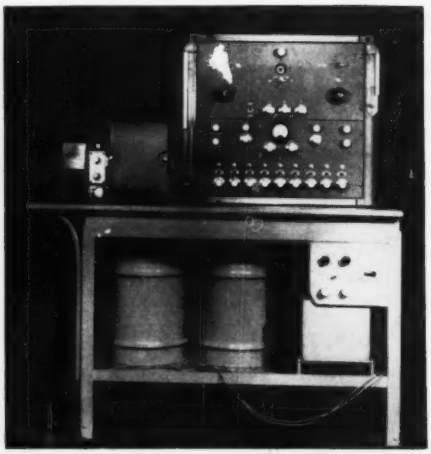

FIG. 11. A photograph of the newly developed electrorheoplethysmograph.

SELECTED APPLICATIONS OF DIGITAL RHEOPLETHYSMOGRAPHY

Basal Component of Digital Flow

It has been of interest for some time to know the basal component of the rate of the pulsating digital blood flow, upon which is superimposed the complemental pulsating increases in flow in association with the heart beat. The basal component in figure 9, for example, is obtained simply by noting the rate of flow at t_o or onset of the pulse cycle in the I_R curve (30 cu. mm./5 ml. part/sec.). Upon this basal rate of flow is superimposed the complemental pulsatile and more rapid rate produced by the heart beat (figs. 13 and 14). The relative roles of the energy from the heart and from the recoil of the vascular walls require study. It has been found that the basal rate of flow is high when the subject is in a hot and humid atmosphere, tends to be low in aortic insufficiency, falls below that at heart level when the part is ele-

* Two pressure transducers, model PT-5, of high sensitivity for digital plethysmography, each with 2 and 10 mm.³ volume calibration plugs, obtained from the Grass Instrument Company, Quincy, Mass.

† Nine type 7-288 galvanometers, natural frequency, 150 c.p.s., 1 type 5-116P4-9 recording oscillograph, 9 trace capacity for operation from 115 v., 60 cycle source, obtained from CEC Instruments, Inc., Pasadena, Calif.

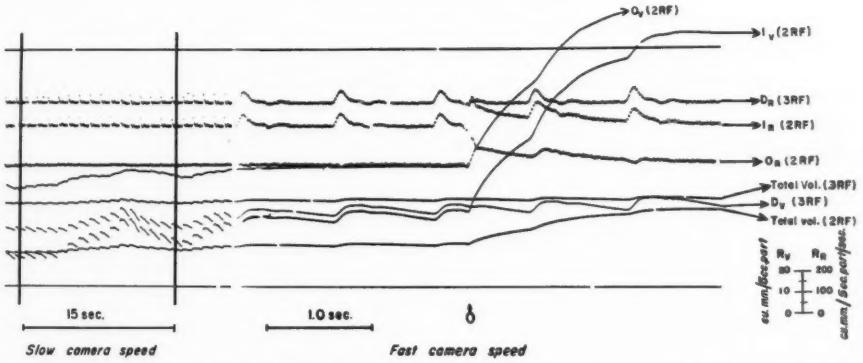

FIG. 12. A normal rheoplethysmogram recorded with the new electrorheoplethysmograph. The volume and rate curves and changes in the total or over-all volumes of the two digits are recorded automatically and simultaneously. The scales for the volume (R_V) and rate curves (R_R) are shown; the ordinate values of rates are 10 times the ordinate values of volume. The ordinate values of the traces of total volume of the digits are one fifth that of the volume pulse traces. By proper standardization of the recording galvanometers, to correct for volume of the part, the linear deflection represents changes in volume directly in cu.mm./5 ml part and changes in rate directly in cu. mm./5 ml part/sec.

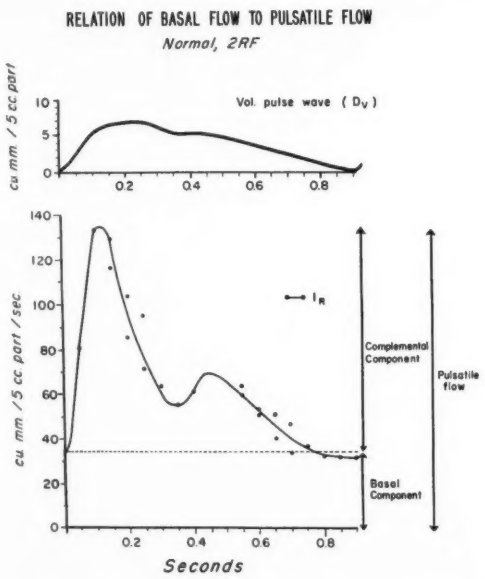

FIG. 13. Curve of the rate of inflow for a normal resting subject. The pulsatile flow is readily divided into the *basal component* and the *complemental component*. The slightly lower level for the rate of inflow at the end of the pulse cycle is due to error caused by leakage past the venous occlusive cuff or a decline in A-V pressure gradient resulting from the blood collected in the digital vessels or both these factors.

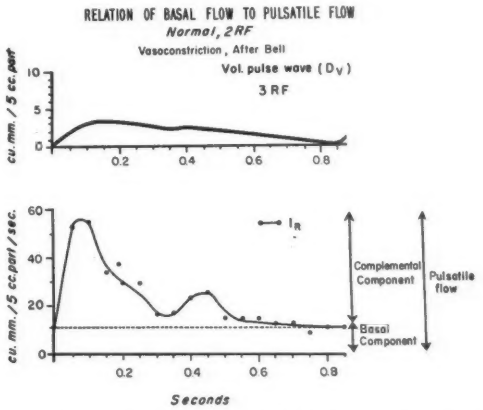

FIG. 14. Curve of the rate of inflow for the same normal resting subject shown in figure 13, in whom vasoconstriction of the digital vessels was produced by sound of a bell. Comparison of the curve with that in figure 13 shows a decline in rate throughout the pulse cycle, involving both the *complemental* and *basal* components of the rate curve or pulsatile flow.

vated 45 cm., is low in Raynaud's disease but high with respect to the maximal rate of flow attained during the systolic phase of the pulse cycle and is decreased by deep inspiration or vasoconstriction produced by psychogenic and neurogenic stimuli, noradrenalin or cold.[11, 18-20] The basal rate of flow of the rheoplethysmogram should be studied further for various

normal and abnormal physiologic states of the central and peripheral circulation.

Mean Rates of Digital Flow

The mean rates of inflow throughout the pulse cycle are easily determined from the volume-time course curves. For example, it is evident from figure 8 that 37 cu. mm./5 ml. part/sec. flowed into the digit during the pulse cycle shown, the duration of which was 0.83 second. The mean rate of inflow, therefore, was 43.1 cu. mm./5 ml. part/sec., which can be readily converted to minutes, hours or any other unit of time or tissue mass. These values, expressed in cu. mm./5 ml. part/sec. can be converted to ml./100 ml. part/min. simply by multiplying the value by 1.2. Since the vascular bed was in a state of equilibrium, the rate of outflow was equal to inflow. From the rates of flow so calculated, one may obtain the mean rate during the particular pulse cycle studied. For more representative values of a particular period of study, the rates for several pulse cycles, including the extremes, must be measured and averaged.

Since the rate of digital flow is known to be extremely variable, the conditions of study must be carefully defined. The atmosphere of the observation room and other environmental factors should be controlled if data are to be compared. The rate of digital inflow increases with ascending alpha and beta deflections and decreases with the descending deflections.

TABLE 1.—*Clinical and Quantitative Rheoplethysmographic Data of One Normal Subject Studied*

Phase	Duration (sec.)	Inflow		Outflow		I_R/O_R
		% Total vol.	Mean rate (cu. mm./5 ml. part/sec.)	% Total vol.	Mean rate (cu. mm./5 ml part/sec.)	
Systole.....	0.33	60.9	67.6	49.5	54.8	1.23
Diastole....	0.52	39.1	27.5	50.5	35.6	0.77

Age	30 yrs.
Blood pressure	90/48
Finger volume	3.67 ml.
Soft tissue volume	3.14 ml.
Bone volume	0.53 ml.
Surface area	10.05 cm.²
Volume inflow per pulse cycle	36.6 cu. mm./5 ml. part (0.73% finger volume)
Basal rate of digital flow	29.4 cu. mm./5 ml. part
Mean rate of inflow	43.1 cu. mm./5 ml. part
Rate of turnover of digital volume at mean rate of inflow	116.0 sec.

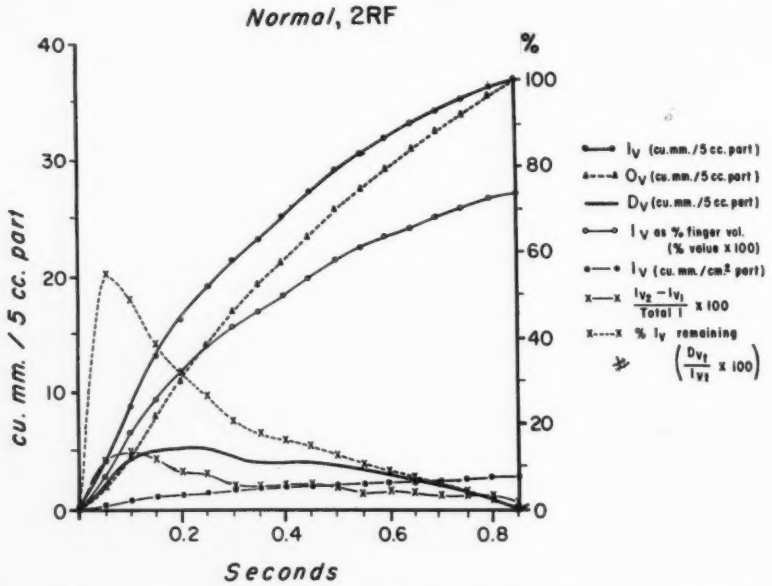

FIG. 15. Various curves obtained from analyses of the rheoplethysmogram of a normal resting subject.

Vasoconstriction produced by fright, orienting reflex, noradrenalin, or cold reduces inflow to a degree directly related to the intensity of the stimulus. Rates of digital flow too low to record have been produced by exposure of the subject to a cool environment of 12 C. Vasodilatation, accompanied by an increase in rate of digital flow, was produced by a hot and humid environmental atmosphere, reflex vasodilatation to heat, sympathectomy or procaine interruption of the sympathetic nerve supply to the digit, pentapyrrolidinium, or hexamethonium. The mean rate of flow was reduced by the presence of Raynaud's disease, crises of Raynaud's phenomenon, severe congestive heart failure, arteriosclerotic obliterative endarteritis and arterial thrombosis, Leriche's syndrome, scleroderma, and other arterial disease states.

Complemental Pulsatile Component of Digital Flow

Superimposed upon an essentially basal rate are the surges in flow that accompany the heart beat, as illustrated in figures 13 and 14. The rheoplethysmogram reveals the time course of these variations and the quantitative and temporal relationships of the *I*, *O* and *D* components throughout the course of the pulse cycle. The configurations of these curves varied considerably under various normal and abnormal physiologic states.[11, 18-20] These relations not only reflect the normal or diseased physio-

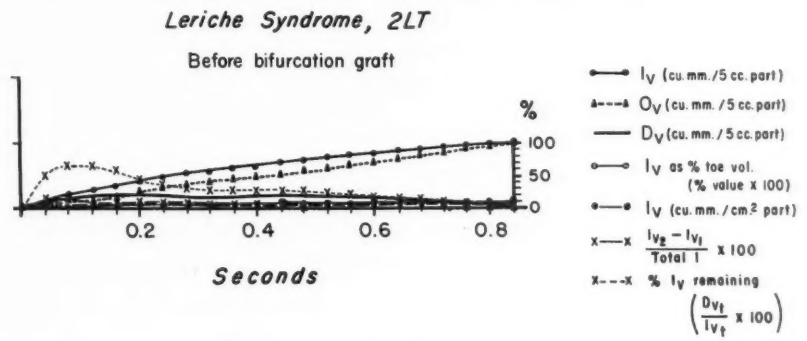

FIG. 16*A*.

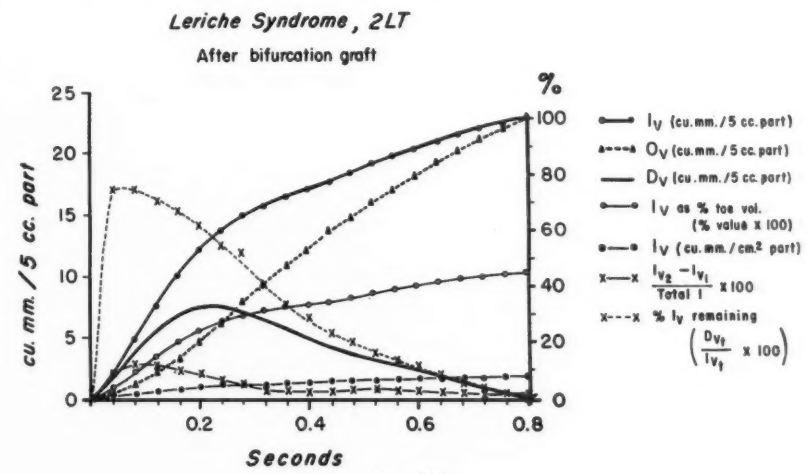

FIG. 16*B*.

FIG. 16. Various rheoplethysmographic curves for the second toe tip of a subject with the Leriche syndrome (*A*) before and (*B*) after graft of aortic bifurcation.

logic state of the circulation but also provide information concerning circulatory function.[18, 19] A study of these rheoplethysmograms can yield interesting data about the central and peripheral portions of the cardiovascular system, including the result of medical and surgical therapeutic procedures employed in the management of disease states of the cardiovascular system (figs. 15, 16*A* and *B*). As stated previously, the associated quantitative changes in the basal and mean rates of flow are revealed in the rheoplethysmograms.

Selected Quantitative Analyses

Since the curves of the rheoplethysmogram are continuous, they are obviously subject to many different types of analyses, some of which have only academic interest, whereas others have, in addition, physiologic significance. No effort is made in this lecture to present a complete series of such analyses, only a selected few being included to illustrate possible approaches.

Time Course of Accumulated Inflow and Outflow as Percentage of Total Digital Inflow and Outflow, Respectively

The time courses during the pulse cycle of the successive accumulated volumes of inflow and outflow at times t can be expressed as percentages of total volumes of inflow and outflow merely by changing the value of the ordinate of the volume-time course curves (I_V and O_V). This is expressed for inflow by the formula:

$$\frac{I_{V_t}}{\text{Total } I_V} \times 100 , \qquad (3)$$

where I_{V_t} is the accumulated inflow at any time t in the pulse cycle and total I_V is the total accumulated volume of inflow during the entire pulse cycle. The same type of formula may be applied to volume of outflow (O_V). These curves make it possible to know at a glance the percentage of total digital inflow or outflow that occurred during systole or during diastole or the moment-to-moment course of flow in detail (fig. 15). Their characteristics vary with physiologic variations, being especially different in some subjects with aortic valvular insufficiency, for example.[19]

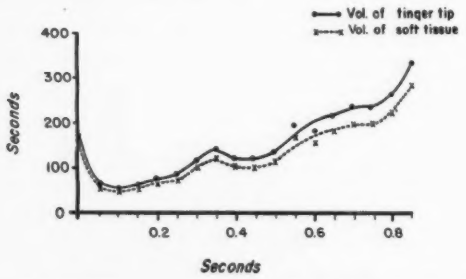

Fig. 17. Time course of the rate of "turnover" of digital blood for the second right finger tip of normal man during the single pulse cycle shown in figure 15. The ordinate represents the length of time that would be required for a volume of blood equal to the volume of the finger tip to flow through the finger tip were the rate of inflow that existed at any moment to prevail throughout the pulse cycle.

Time Course of Rate of "Turnover" of Digital Blood

An estimate of the rate of digital blood flow can be expressed as the time required for a volume of blood to flow through the digit that is equal to the total volume of the digit, volume of the digital soft tissue, or volume of the digital bone for the mean rate of flow or for the rate of flow that prevails at any moment during the pulse cycle (fig. 17). This method of expression emphasizes further the rapid rates of digital flow. It is evident from figure 17 that if the maximal rate of flow in that particular pulse cycle were to prevail constantly, a volume of blood equal to the volume of the entire fingertip would circulate through the fingertip in 50 seconds. If the minimal rate of inflow were to prevail, however, 175 seconds would be required for a volume of blood equal to the digital volume to circulate through the digit. Inspection of the curves in figure 17 reveals other interesting details. The higher values at the end of the pulse cycle than at the beginning are the result of a decline in the A-V pressure gradient and possibly leakage past the occluding cuff, factors discussed earlier in this presentation.

Such curves reveal great differences in the peripheral circulation in the normal and various disease states, too numerous to illustrate here. These curves should make possible an approach

to estimation of the state of digital circulatory reserve.

Time Course of Inflow Remaining as Percentage of Accumulated Blood Flowing in at any Moment in the Pulse Cycle

The time course of the percentage of accumulated inflowing blood that remains in the digit at any time t can be calculated from the equation:

$$\% I_{V_t} \text{ remaining} = \frac{I_{V_t} - O_{V_t}}{I_{V_t}} \times 100 = \frac{D_{V_t} \times 100}{I_{V_t}}. \quad (4)$$

I_{V_t} and O_{V_t} may be measured at successive 0.05 second periods of time throughout the pulse cycle to produce a satisfactory curve (fig. 15). This curve may serve as a rough index of the duration of time that blood remains in the tissues for purposes of chemical and thermal exchange, but, unfortunately, the blood escaping is not a portion of that entering at the same moment. For example, early in the pulse cycle the subject with aortic insufficiency often retained almost 100 per cent of the inflow, a situation not yet observed in normal man under comparable experimental conditions. These relations between inflow and outflow are considered to represent effects of the critical closing and opening phenomena described by Burton.[21]

Time Course of Change in Volume Inflow as Percentage of Total Volume Inflow

The changes in volume of inflow from one 0.05 second period to the next during a single pulse cycle may be expressed as percentage of total digital inflow during the pulse cycle to learn the time course of the change in volume inflow as percentage of total volume inflow. The values were derived from the expression:

$$\frac{I_{V_2} - I_{V_1}}{\text{Total } I_V} \times 100, \quad (5)$$

where $I_{V_2} - I_{V_1}$ is the inflow from t_1 to t_2, measured at 0.05-second intervals in the pulse cycle, and total I_V is total inflow for the entire pulse cycle.

This ratio is concerned with inflow only and is not influenced by simultaneous outflow. These curves (fig. 15) reveal the time course of the variation in total inflow delivered to the digit during successive intervals in the pulse cycle. For example, during one 0.05-second period almost 10 per cent of the total inflow occurred, whereas less than 5 per cent occurred during most of the other 0.05-second intervals of the pulse cycle. The importance of these quantitative variations in inflow upon the rate of metabolism in the tissues is unknown. The metabolic rate may oscillate in some way with respect to the rate of inflow.

The remarkable aspect of these curves is their striking similarity in magnitude and configuration despite wide variations in normal and abnormal physiologic states, for example, vasoconstriction, vasodilatation, and disease of the cardiovascular system. Apparently the moment-to-moment percentage of total volume of blood flowing into the fingertip during a pulse cycle is fairly constant even in the presence of large variations in peripheral and central circulation.[20] One of the main exceptions to this general rule was observed in the curves of a patient with aortic insufficiency,[19] but surely other exceptions exist. Although the maximal value during the pulse cycle was approximately 10 per cent of total inflow for most pulse waves studied and the magnitude of the percentage values was remarkably similar during the same relative moments in the pulse cycle, the maximal value in some subjects with aortic insufficiency was as high as 20 per cent. Many more records must be carefully analyzed to define consistencies and peculiarities in this type of curve.

General Discussion

Many other relations and analyses, which may elucidate cardiovascular physiologic phenomena and reveal early pathologic activity, are available in the continuous curves of the rheoplethysmograms (RPG). These simultaneous time-course curves permit a study of temporal interrelations during a pulse cycle, in which the functions of the arterial and venous sides of the digital vascular bed may be differentiated to some extent. Events in inflow

and outflow may be simultaneously correlated at any moment during the pulse cycle. Since the RPG shows the rate of outflow to fluctuate considerably, the venous side of the digital vessels must pulsate correspondingly.[11] These curves readily reveal mean rates and wide variations in basal rates of flow under normal and abnormal physiologic variations, the magnitude of which has been unknown and only conjectured.

The RPG readily shows when leakage past the occluding cuff occurs or when changes in the A-V pressure gradient produce definite errors in measurements of flow, important information for proper quantitative evaluation of the data. The mean rates of digital flow, as measured rheoplethysmographically, are higher than those generally reported by other methods, probably due to elimination of errors caused by leakage past the occluding cuff, decline in the A-V pressure gradient and other factors.[11]

The average rate of flow for the finger of normal man at rest was compared with that for equal volumes of vital organs with known high rates of blood flow (fig. 18) and, under comfortable environmental conditions, was found to be of about the same magnitude as that for the liver, brain, and myocardium of the left ventricle and to be several times the average flow for the whole body. Reasons for this high rate of digital flow are unknown but may be related to thermal regulation, repair of digital tissue, which is almost constantly subjected to physical trauma, and to the large blood supply necessary for tactile sensory function. These sensitive organs may require a rich supply of blood for highly discriminatory function in touch, the fifth sense, so important to man's daily life. The high rate of digital flow varies considerably, practically reaching zero levels when the subject is in a cool atmosphere and rising to high levels when the subject is in a hot and humid environment. Paresthesia of the fingertips in cold environment indicates the importance of adequate circulation to the digits. The "hunting phenomenon," described by Sir Thomas Lewis for cold digits, may reflect an effort to maintain adequate circulation to the digital tactile organs with minimal thermal loss. Such problems require study.

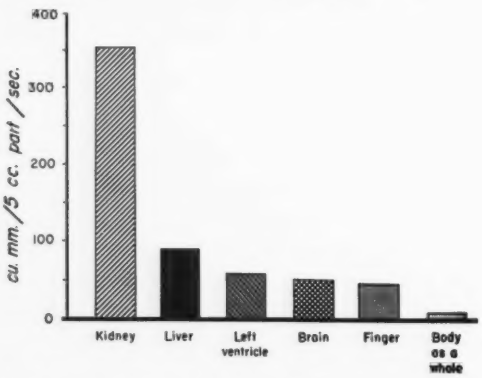

FIG. 18. Rate of digital flow in normal man compared with rates of flow reported in the literature by others for selected vital organs of man.

The rheoplethysmographic method requires further development, especially that involving the problem of the artifact and the capacity of the reservoir vessels. It can be of value not only in a study of physiologic phenomena but also in evaluation of drugs and therapeutic procedures concerned with the circulation. By this method actions upon the arterial and venous segments of the circulation can be approached in the intact circulation of man and other animals.

These discussions have purposely avoided the presentation of studies of specific disease states, pharmacologic responses in the cardiovascular system, effects of therapeutic procedures on the cardiovascular system, diagnostic procedures and other physiologic reactions of the cardiovascular system reflected in the RPG, but some such studies have already been reported.[11, 18-20] No attempt has been made to define the variations and limitations of the normal RPG. However, with existing knowledge of digital plethysmography, calorimetry and thermometry, as well as the behavior of the cardiovascular system, more rapid understanding of rheoplethysmography may be obtained.

Although the great reactivity and variability of the digital circulation has been considered objectionable by some for the study of aspects of the peripheral circulation, these are actually favorable factors and should be exploited.

Simplicity in use of a digit and its lack of muscle, with separate circulation, is an advantage. Furthermore, the tips of the digits are complex organs that reflect vascular disease early and extensively. The methods of digital rheoplethysmography are simple to employ and are dependable, yet disturb the subject relatively little during the period of study.

For simplification, symbols have been introduced in the field of rheoplethysmography that are simple, obvious, and readily learned.[11, 18-20] With the development of an electrorheoplethysmograph with difference and differentiating circuits, calculations of the various curves have been simplified or eliminated. However, complex apparatus is not essential; ordinary conventional plethysmographic equipment can be adapted for rheoplethysmography. Regardless of the methods used in digital rheoplethysmography, accuracy and methodic, deliberate approaches must be developed and used for satisfactory results. Errors in the methods, extent of the variations, conditions of the subject and his physiologic state, as well as conditions of the environment and the observations, must be considered for adequate evaluation and interpretation of the data.

Plethysmography, and especially rheoplethysmography, like electrocardiography, requires training, knowledge of the subject, and experience. When properly employed, rheoplethysmography has a great deal more to offer in the study of the cardiovascular system than conventionally employed digital plethysmography, but its value in clinical practice has not yet been established. At present it does not supplant simple clinical procedures; it has only supplementary value, if any at all, in a limited number of subjects in the everyday management of cardiovascular diseases. Its potentialities, however, are evident.

Summary

This lecture briefly summarizes the principles of digital rheoplethysmography, which records simultaneously the time course of the volume, rate, and acceleration of inflow, outflow, and difference between inflow and outflow for a single pulse cycle, as well as the basal rate of flow. The mean rate of flow during a single pulse cycle is readily obtainable. Although problems remain to be solved, the method introduces a new approach to a quantitative analysis of the peripheral circulation of intact man. A specially constructed electrorheoplethysmograph permits simultaneous recording of nine traces and reduces considerably the need for manual construction of curves and calculation of data.

Rheoplethysmography permits a study of normal and abnormal physiologic states of the peripheral circulation, with its pharmacologic responses, in intact man and makes possible simultaneous study of the arterial and venous sides of the circulation. It can be applied to organs other than the digits of man.

Summario in Interlingua

Iste discurso summarisa brevemente le principios de rheoplethysmographia digital, que registra simultaneemente le curso temporal del volumine, prorata, e acceleration de influxo, effluxo, e differentia inter influxo e effluxo pro un sol cyclo pulsar como etiam le prorata basal del fluxo. Le prorata median del fluxo durante un sol cyclo pulsar es facilemente obtenibile. Ben que il ha problemas que remane a resolver, le methodo introduce un nove base pro le analyse quantitative del circulation peripheric de humanos intacte. Un specialmente construite electrorheoplethysmographo permitte le registration simultanee de 9 traciamentos e reduce considerabilemente le necessitate del construction manual de curvas e del calculation de datos.

Rheoplethysmographia permitte le studio de normal e anormal statos physiologic del circulation peripheric (con su responsas pharmacologic) in humanos intacte e rende possibile le studio simultanee del aspectos arterial e venose del circulation. Illo pote esser applicate a organos altere que le digito de humanos.

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Treatment of the Low-Salt Syndrome in Congestive Heart Failure by the Controlled Use of Mercurial Diuretics

By ALBERT L. RUBIN, M.D., AND WARREN S. BRAVEMAN, M.D.

The production of the low-salt syndrome in cardiac patients with refractory congestive heart failure is generally attributed either to fluid retention with electrolyte dilution or to excessive salt loss, induced by the frequent administration of mercurial diuretics. The former is often the important etiologic factor. In a study of a group of 25 refractory cardiac patients with normal plasma electrolyte patterns, a hyperchloremic acidosis was produced to restore a responsiveness to mercurial diuretics. During the mercurial-induced diuresis that followed, the urinary sodium concentration was significantly lower than the plasma sodium concentration in all instances. From these observations, a method of treatment of the low-salt syndrome, utilizing mercurial diuretics seemed feasible. This regimen was successfully carried out in two hyponatremic patients with return of plasma sodium to normal and striking clinical improvement.

IN cardiac patients with fluid retention, two types of electrolyte imbalance have been associated with a transient refractoriness to mercurial diuretics. One of these is hypochloremic alkalosis, and the other is hyponatremia in association with hypochloremia, the "low-salt syndrome."

The former is a well-defined clinical entity[1] that sometimes occurs in the course of vigorous treatment of the edematous cardiac patient with salt restriction and protracted daily injections of a mercurial diuretic agent. Hypochloremic alkalosis may occur prior to the attainment of optimal body weight. Responsiveness to mercurial diuretics is restored in this situation when the hypochloremia is corrected by the administration of ammonium chloride.

The latter electrolyte imbalance, the "low-salt syndrome," can be present in a number of disease states. These have been discussed recently by Danowski and his associates[2] who call them the "low-salt syndromes" and classify them according to total stores of extracellular sodium—decreased, intact, and increased. The patients discussed in this article would fall into that group demonstrating the "low-salt syndrome" with increased sodium stores and congestive heart failure.

The "low-salt syndrome," as originally described by Schroeder[3] consisted of (1) drowsiness, weakness, and lethargy, (2) loss of appetite, (3) nausea and vomiting and occasionally abdominal or muscular cramps. These symptoms occurred in a setting of (1) a successive depression of urinary volume, (2) decreased urinary excretion of chloride ion, not increasing after mercurial diuretic administration, (3) progressive gain in body weight, (4) rising nonprotein nitrogen content of the blood, and (5) hyponatremia and hypochloremia. The author reported two mechanisms by which this syndrome could be produced: by retention of water and dilution of electrolytes, and by excessive depletion of the body salt, usually associated with the use of mercurial diuretics. The former mechanism is well recognized, having been seen many times in postoperative surgical patients given parenteral glucose in water,[4] and its significance as an etiologic factor in the production

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of the "low-salt syndrome" has received recognition.[5, 6]

With regard to the latter mechanism, the question may be raised whether the data establish that mercurial diuretics contribute to the development of the clinical state described. In the original paper on the "low-salt syndome," only urinary chloride ion concentration was measured. Sodium excretion was not determined. Measuring urinary chloride concentration alone gives a false conception of sodium losses. A greater proportion of the chloride ion than of the sodium ion in the extracellular fluid is excreted in the urine after the administration of mercurials, apparently because such agents act primarily on the chloride ion.[7] All the subjects showed significantly positive daily water balance, and, in all cases but one, mercurial diuretics were administered very infrequently and intermittently. Only one of the cases reported showed a significant diuresis as judged by weight loss, after the administration of hypertonic saline solution to correct the electrolyte imbalance. Many did not lose as much weight after therapy as they had gained during their period of oliguria. For these reasons all the cases could represent examples of extracellular fluid expansion with electrolyte dilution, and no direct evidence is presented to incriminate mercurial diuretics as etiologic agents. To state unequivocally that hyponatremia results from the administration of mercurial diuretics, it should be necessary to show that urinary sodium concentrations in the diuresis following drug administration exceeds the plasma concentration of sodium, in a setting where the fluid intake is restricted to approximate the patient's insensible loss (e.g., 1 kilogram of weight loss is equivalent to 1 L. of urine output). To our knowledge, this has never been demonstrated.

In our experience, most patients with refractory edema due to heart failure have normal plasma electrolyte concentrations.[8] At this stage in the natural history of their heart disease, these patients are unable to handle water as well as salt. This is not generally appreciated, and while salt intake is rigidly restricted, fluid intake is not. The result is fluid retention, further expansion of extracellular fluid volume, and consequently electrolyte dilution.

Overhydration with resultant expansion of the extracellular fluid volume and dilution of electrolytes would appear to be the most important etiologic factor in the production of this syndrome, which might better be termed the "dilution syndrome."

In 25 refractory cardiac patients with normal plasma sodium and chloride concentrations in whom a hyperchloremic acidosis was produced by means of Diamox (acetazokamide) and ammonium chloride,[8] a responsiveness to mercurial diuretics was restored. In all these patients the urinary sodium concentration during the mercurial-induced diuresis was

TABLE 1.—*Plasma and Urinary Sodium and Chloride Concentrations and Weight Loss in a 24-Hour Period of Responsiveness to the Administration of a Mercurial Diuretic in a Setting of Hyperchloremic Acidosis. In Every Instance the Sodium Concentration in the Urine Is Significantly Lower Than the Plasma Concentration*

Pt.	Plasma Na^+	Urine Na^+	Plasma Cl^-	Urine Cl^-	Wt. Loss (lbs.)/24 hours
	mEq/L				
E. G.	137	112.5	118	158	7.9
	140	99	123	151	4.0
	140	98	123	150	6.5
I. R.	131	115	116	154	10.5
	131	95	115	175	5.5
L. B.	137	45	120	154	10.0
	137	91	116	151	6.0
	137	77	116	155	5.0
W. N.	136	98	120	165	11.0
	136	81	118	158	5.5
	136	82	117	162	7.0
	135	90	120	160	8.0
	138	72	116	167	3.0
E. B.	134	82	119	146	10.0
	135	91	119	161	4.5
	136	57	115	116	5.0
	136	66	115	140	4.5
T. J.	136	90	116	149	10.0
	135	82	111	136	3.5
	135	68	110	123	4.5
S. B.	142	85	117	133	7.5
	137	93	107	135	5.0
G. B.	137	78	118	129	5.0
	138	87	116	142	4.5
B. E.	137	113	129	132.8	6.0

significantly lower than the plasma sodium concentration. Table 1 lists the plasma and urine sodium and chloride concentration and the weight loss in pounds that occurred in a 24 hour period after the administration of 2 ml. of Mercuhydrin (meralluride) in the setting of a hyperchloremic acidosis, on 40 separate patient days. Note that the urine is always hypotonic for sodium with respect to the plasma, and that the concentration of chloride in the urine markedly exceeds that of sodium.

In these patients, plasma sodium concentration remained within normal limits, probably reflecting ion shifts between intracellular and extracellular fluid compartments. In patients with hyponatremia, it was theorized that in a similar situation, plasma sodium concentration might rise toward normal, if homeostatic mechanisms tending to regulate body sodium were functioning. For, if 1 L. of edema fluid is removed from the body with a sodium concentration less than that in the plasma, *and is not replaced by fluid administration* (i.e., the patient loses 1 Kg. in weight), extracellular fluid sodium concentration should rise.

It appeared to us, developing the premise that this syndrome represented a primary dilution phenomenon, that the aim in therapy should be the mobilization of excess fluid in the expanded extracellular fluid space, rather than elevation of the extracellular fluid sodium content. Accordingly, a group of five patients with heart disease, congestive failure, and refractory fluid retention, who showed azotemia, oliguria, anorexia, and nausea, and who had a marked hyponatremia and hypochloremia were treated with a regimen that had been successful in restoring responsiveness to mercurial diuretics in cardiac patients with refractory fluid retention who had normal plasma electrolyte patterns. This regimen, which utilizes Diamox and aqueous ammonium chloride, has previously been described in detail.[8] No attempt was made to alter plasma sodium concentrations. In the setting of a hyponatremia, an elevated plasma chloride concentration, lowered blood pH, and lowered carbon dioxide combining power, the daily administration of Mercuhydrin resulted in a marked and sustained diuresis in all five cases, during the course of which plasma sodium concentration returned to normal.

Two cases from this group have been selected for this report on the basis of the completeness of their data.

Methods

1. Each patient selected was carefully evaluated to insure adequate digitalization and to rule out complicating disease, such as thyrotoxicosis, infection, or pulmonary infarction.
2. Fluid intake was restricted to less than 1500 ml., and salt intake to 2 grams or less daily.
3. Plasma pH, carbon dioxide combining power, chloride, sodium and potassium, urine output, and urine sodium, potassium, and chloride concentrations were determined daily.
4. Aqueous ammonium chloride was given daily in 5 divided doses of 2 grams each, and Diamox in a single daily dose of 750 mg. by mouth. If the patient's initial carbon dioxide combining power was elevated (as in case 2), Diamox was given without ammonium chloride until its diuretic effect had waned, and then ammonium chloride was added.
5. When the chloride concentration in the urine had risen over 40 milliequivalents per liter, Diamox was discontinued and 2.0 ml. of Mercuhydrin were given intramuscularly daily. Ammonium chloride administration was continued throughout the period during which Mercuhydrin was given.
6. Laboratory methods used for determinations of plasma pH and carbon dioxide combining power, plasma and urinary sodium, potassium, and chloride have been previously described.[8]

Case Reports

Case 1. S. S., a 51-year-old white luncheonette owner, was admitted to the New York Hospital for the fifth time in severe congestive heart failure. He had first been hospitalized 2 years before with a myocardial infarction. Subsequent admissions were for control of cardiac decompensation which had its onset 6 months after the occurrence of the myocardial infarction. He was maintained on digitalis, a salt-poor diet, and restricted activity.

For 3 weeks prior to his present admission, his dyspnea and orthopnea had become progressively more severe, despite continued use of digitalis, frequent mercurial injections, ammonium chloride, bed rest, and salt restriction.

Physical examination on admission revealed a lethargic, severely dyspneic and orthopneic, cyanotic, acutely ill man with a blood pressure of 180/100, pulse 100 (regular), respiratory rate 30 per minute, temperature 39.2 C. He showed distention of the neck veins, bilateral pleural effusion, rales in both lung fields, cardiomegaly with a gallop rhythm, hepatomegaly, and 4 plus pitting ankle and sacral

TABLE 2.—*Medications, Daily Weight Change, Plasma and Urine Electrolyte Concentrations, and Fluid Intake and Output in Case 1*

Day	Medication	Blood Urea Nitrogen mg. %	Wt. Change lbs.	Plasma					Urine						Intake cc./24 hr.	Output cc./24 hr.
									Na^+		Cl^-		K^+			
				Ph	Na^+ mEq /L	Cl^- mEq /L	Co_2^- mM /L	K^+ mEq	Conc. mEq /L	Total mEq/ 24 hr.	Conc. mEq /L	Total mEq/ 24 hr.	Conc. mEq /L	Total mEq /24 hr.		
1–20		20–67	142–169		131–112	98–87	25–21	4.6–6.6							2300 O.D.	800 O.D.
21	Diamox, NH_4Cl	27	168–168	7.43	120	94	22.6	5.8	1.8	0.6	12.8	4.2	78	25.3	500	325
22	Diamox NH_4Cl		168–168	7.39	120	99	19.6	5.2	1.3	0.9	17.4	11.4	76.5	49.8	1100	650
23	Diamox, NH_4Cl		168–169	7.37	122	106	15.2	5.1	1.7	1.6	38.6	36.1	71.5	66.9	900	935
24	Diamox, NH_4Cl		169–168.5	7.34	120	107	14.8	4.4	7.2	5.1	43	30.1	50.8	35.6	700	700
25	Merc, NH_4Cl		168.5–153	7.27	120	114	8.4	5.0	87.5	622	118.4	842	26.5	188	760	7100
26	Merc, KCl, NH_4Cl	19	153–134	7.34	128	112	12.2	3.0	98	840	136	1163	19	165	1000	8600
27	Merc, KCl, NH_4Cl		134–126	7.45	132	106	24.8	3.3	80.8	209	139	358	32	83	1000	2600
28–35	Merc, 2x	18	126–120	—	132	102	28	3.5	—	—	—	—	—	—	—	—

edema. Initial laboratory findings included 2 plus albuminuria, hematocrit value 55 per cent, venous pressure (antecubital vein) 300 millimeters of saline, circulation time (decholin, arm to tongue) 40 seconds, blood urea nitrogen 41 mg. per cent, sodium 131 mEq., chloride 98 mEq., and carbon dioxide 25 mM per liter.

The patient was initially treated with complete bed rest, 1 Gm. salt diet, oxygen, phlebotomy, and was given additional digitalis until minor toxic symptoms appeared. Despite these measures, he showed no improvement. Table 2 is a tabulation of the daily weight, intake and output, plasma and urine electrolyte concentration, and medications given in this case. After 10 days his weight had risen, and his urine output had fallen below 1000 ml. per day. The blood urea nitrogen was 67 mg. per cent. The plasma sodium had fallen to 122 mEq. and the plasma chloride to 87 mEq. per liter.

During the next 2 weeks, 5 per cent hypertonic saline was administered intravenously in amounts of 100 to 200 ml. on 6 different occasions in an attempt to correct the hyponatremia and hypochloremia. At the end of this period the patient had gained 13 pounds, showed anasarca, and was symptomatically worse. Plasma sodium concentration was 112 mEq. and plasma chloride concentration was 98 mEq. per liter.

At this time, a review of the patient's clinical course showed that in this 20-day period, a significantly positive daily water balance was present. Fluid intake had averaged 2300 ml. daily, while his urine output averaged 800 ml. daily. During this period, the patient had been afebrile and had not perspired excessively. The major factor in his hyponatremia and hypochloremia was felt to be dilution, and it was decided that therapy should be directed primarily toward mobilization of this excess total body water.

Accordingly, the patient was given 750 mg. of Diamox in a single dose by mouth and 10 Gm. of aqueous ammonium chloride in 5 divided doses daily for 4 days. Fluid intake was restricted to approximate his urine output plus estimated insensible loss. During this 4-day period of Diamox and ammonium chloride administration, his weight did not change. A hyperchloremic acidosis was produced. The plasma pH fell from 7.43 to 7.27 and plasma chloride rose from 94 to 114 mEq. per liter. Carbon dioxide combining power fell from 22.6 to 8.4 mM per liter. No symptoms of acidosis developed. Plasma sodium remained low at 120 mEq. per liter, and plasma potassium stayed within normal limits. Urine output averaged 850 ml. daily with very low-sodium content. Urine chloride content, initially low, rose as the plasma chloride level increased (table 2 and fig. 1).

In this setting of a hyponatremia and hyperchloremic acidosis, Mercuhydrin (2 ml. intramuscularly) was administered daily for 5 days. Ammonium chloride administration was continued, and potassium chloride was given on the second and third days. A striking diuretic response was achieved, with a peak urine output of 8½ liters occurring on

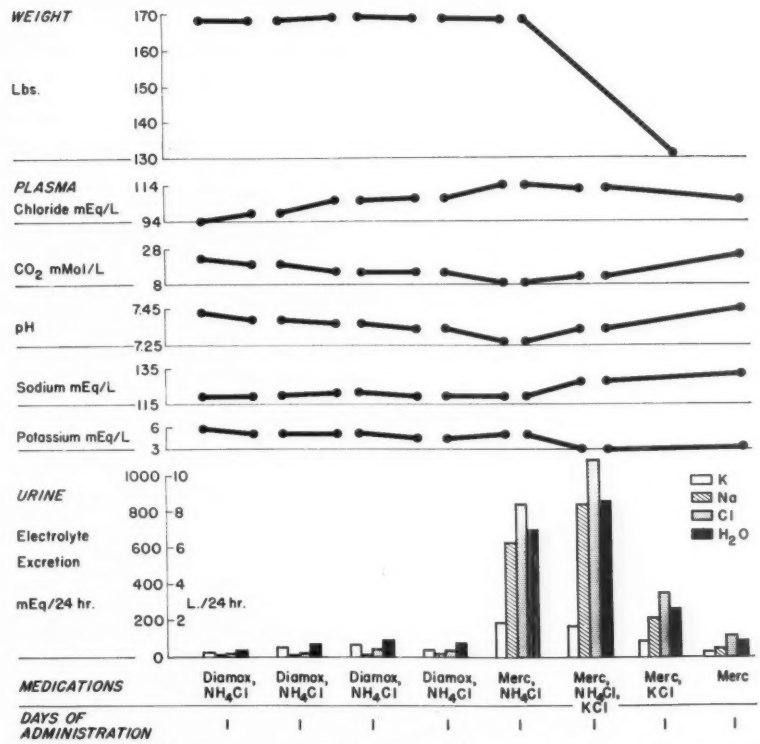

FIG. 1. Case 1. A graphic representation of the course of observation. On the ordinates are listed the body weight, plasma electrolyte concentrations and pH, and urine electrolyte excretions and output for each 24-hour period. On the abscissas are listed the medications given and the number of days each medication, or combination of medications, was given.

the second day of mercurial administration. In this 3-day period, the patient lost 42 pounds in weight. Total daily urinary excretion of sodium and chloride was high, with chloride content exceeding sodium on each day. *However, it is most significant to note that with respect to the plasma, the urine each day was hypotonic so far as sodium was concerned.* In this 3-day period, the hyponatremia was corrected, the plasma sodium rising from 120 to 132 mEq. per liter. The patient's electrolyte pattern at the end of this time had returned almost to normal (sodium 132 mEq., potassium 3.4 mEq., chloride 102 mEq., carbon dioxide 28 mM per liter). The blood urea nitrogen had fallen to 18 mg. per cent. Clinically he was dramatically improved and subsequently he could be allowed out of bed. Figure 1 is a graphic representation of the patient's response to this regimen.

This improvement continued in the next 2 weeks with a further 6-pound weight loss on mercuhydrin alone.

In his sixth hospital week, while arrangements for further care at home were being made, the patient died quietly while asleep, apparently from a myocardial infarction or pulmonary embolism.

Case 2. L. T., a 53-year-old white male clerk was admitted to the New York Hospital in pulmonary edema. He had a 20-year history of hypertension and chronic lung disease. When admitted to a hospital 1 year before, he was in chronic heart failure and responded well to a regimen of digitalis, salt restriction, and mercurial diuretics. At that time the laboratory findings included a hematocrit value of 37, a blood urea nitrogen of 15 mg. per cent, and carbon dioxide combining power of 36 mM per liter. The electrocardiogram showed a pattern of left ventricular hypertrophy. Roentgenogram of the chest was compatible with pulmonary emphysema. Gastrointestinal and hematologic work-up revealed no explanation for the low hematocrit value. The patient did well on an ambulatory regimen of digitalis, mercurials, and a salt-poor diet until 2 months prior to his present admission, at which time he had an upper respiratory infection, and dyspnea and ankle edema recurred. During the 2 weeks prior to admission, shortness of breath and ankle swelling

increased despite mercurial injections twice a week. During this period his fluid intake was high and salt intake was drastically curtailed.

Physical examination on admission revealed a blood pressure of 180/110, pulse 100 (regular), rate 30 per minute, temperature 37.2 C. He seemed both acutely and chronically ill, and was disoriented, dyspneic, and cyanotic. There was grade III retinopathy. Neck veins were distended. The chest had an increased anteroposterior diameter, was hyperresonant to percussion, had diminished tactile fremitus, and fine, medium, and coarse rales throughout. His heart was enlarged to the anterior axillary line, and an apical systolic murmur was present. The liver was felt 5 fingerbreadths below the right costal margin. Ascites and 4 plus ankle and sacral edema were present.

Laboratory findings on admission included urine specific gravity of 1.012 with 2 plus albuminuria, a hematocrit value of 37 per cent, and a blood urea nitrogen of 29 mg. per cent. The venous pressure was 200 mm. of saline in the antecubital vein, and the circulation time was 18 seconds (arm to tongue, decholin). Plasma sodium concentration was 120 mEq. per liter. Roentgenogram of the chest revealed cardiomegaly and was compatible with pulmonary emphysema. The electrocardiogram showed a pattern suggestive of left ventricular hypertrophy in the precordial leads, with no axis deviation and clockwise rotation.

With the history of salt restriction, oliguria, weight gain, and high fluid intake, it was felt that the hyponatremia was the result of dilution rather than inordinate urinary losses of salt. Table 3 lists the daily weight, intake and output, plasma and urine electrolyte concentrations, and medications given in this case.

The patient was placed on bronchodilators, bed

TABLE 3.—*Medications, Daily Weight Change, Plasma and Urine Electrolyte Concentrations, and Fluid Intake and Output in Case 2*

Day	Medication	Blood Urea Nitrogen, mg. %	Wt. Change, lbs.	Plasma					Urine						Intake cc./24 hr.	Output cc./24 hr.
									Na^+		Cl^-		K^+			
				Ph	Na^+ mEq/L	Cl^- mEq/L	CO_2^- mM/L	K^+ mEq	Conc. mEq/L	Total mEq/24 hr.	Conc. mEq/L	Total mEq/24 hr.	Conc. mEq/L	Total mEq/24 hr		
1	Merc	29			120		37	4.6								
2	Diamox, 750 mg.															
3	Diamox		156–154	7.47	120	81	33	3.5	9.3	14.0	2.8	4.2	46.3	69.5	High	2650
4	Diamox		154–148.3	7.44	120	83	32.9	3.0	6.0	21.0	3.6	12.6	31.5	110		3500
5	Diamox		148.3–147	—					22.0	50.6	6.0	13.8	16.5	38		2300
6	Diamox, KCl	17	147–145.4	7.41	122	87.6	30.4	3.4	16.5	51.2	6.0	18.6	18.8	58.3		3100
7	Diamox, KCl		145.4 144.9						12.5	38.8	5.4	16.7	23.8	73.8		3100
8	Diamox, NH_4Cl, KCl		144.9–144	7.35	125	93.8	29.5	3.4	6.0	17.4	4.2	12.2	23.5	68.2	2.0 gm. salt	2900
9	Diamox, NH_3, KCl								4.0	7.6	6.0	11.4	31	58.9		1900
10	Diamox, NH_3, KCl		144–144						6.0	10.2	30.4	61.9	57.5	97.8		1700
11	Diamox, NH_3, KCl		144–144						11.5	19.5	78.4	133.3	66	112.2		1700
12	Merc, NH_4Cl, KCl		144–143	7.34	125	102	21.3	4.2	31.5	60	121	230	59.5	113	Fluids restricted to	1900
13	Merc, NH_4Cl, KCl		143 ↓						65.3	274.3	114.8	482.2	45.3	190.3	1500 cc.	4200
14	Merc, NH_4Cl, KCl		134						51	193.8	130.2	494.8	54.8	208.2	↓	3800
15	Merc, NH_4Cl, KCl	19	134–129	7.36	131	100	23	3.4								4500
15–17	Merc, NH_4Cl, KCl		129–118.3		[138	104	25	4.9]							↓	

rest, salt restriction, and was given a mercurial diuretic the first day. He lost no weight during the first 24 hours, although his pulmonary status improved. He was then given 750 mg. of Diamox by mouth daily for 7 days with 5 Gm. of potassium chloride on the fifth and sixth days. During this time, due to a misunderstanding, fluid intake was not restricted. The patient responded with a diuresis, losing 7.2 Kg. in weight. The major weight loss, 6 Kg., occurred in the first 4 days, during which time the plasma carbon dioxide combining power fell from 37 to 29.5 mM per liter. This initial response to Diamox alone is attributable to the high plasma bicarbonate content. During this period of diuresis the urine contained very little chloride, sodium content was low, and potassium high. At the end of this 6-day period, the plasma sodium was 125 mEq., chloride 93.8 mEq., carbon dioxide combining power 29.5 mM, and potassium 3.4 mEq. per liter. The plasma pH was 7.35, falling from pre-treatment level of 7.47 (fig. 2).

For the next 4 days Diamox and potassium chloride were continued, and 8 grams of aqueous ammonium chloride in 4 divided daily doses were added. During this period the plasma sodium remained at 125 mEq. , and the carbon dioxide combining power fell to 21.3 mM per liter. The plasma pH was 7.34 at the end of this period. No significant weight change occurred. Through error, fluid restriction had not yet been instituted. Urinary output averaged 1800 ml. daily.

Urinary chloride excretion, initially low, increased 11 fold in daily stepwise fashion as the plasma chloride concentration returned to a normal level. In this setting of hyponatremia and a normal plasma chloride concentration, Diamox administration was stopped, fluid intake was restricted to 1500 ml. a day and Mercuhydrin, 2.0 ml. intramuscularly, was administered daily for 7 days. Ammonium chloride and potassium chloride supplements were continued throughout this period. A sustained diuresis ensued and the patient lost 25.5 pounds in weight. During this period the urine contained a high concentration of chloride ion and a moderately high concentration of sodium ion (table 3). *However, each liter of urine was significantly hypotonic for sodium with respect to*

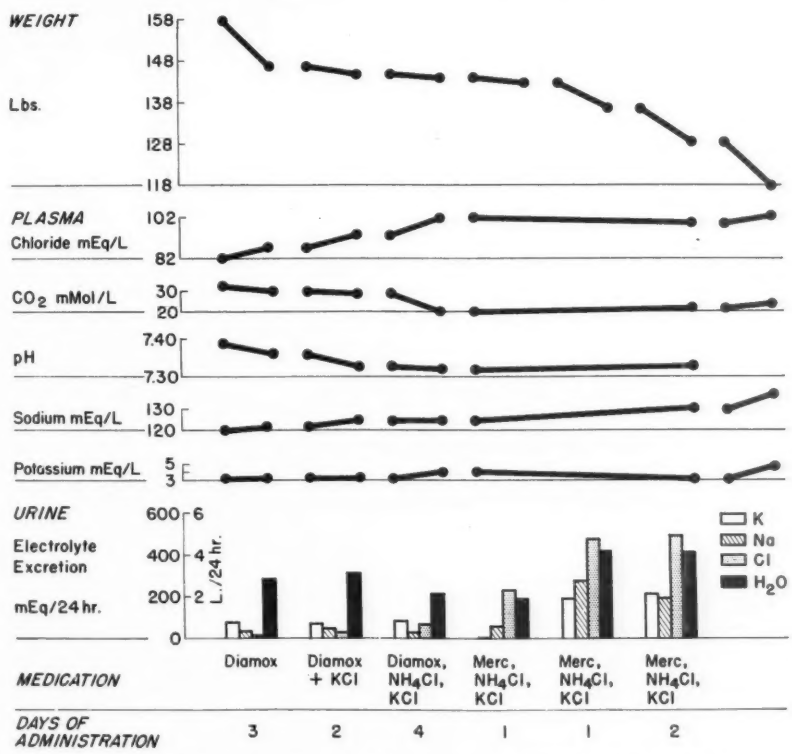

FIG. 2. Case 2. A graphic representation of the course of observation during which the regimen described in the text was used. Where the days of drug administration are more than one, the urine electrolyte excretions and urine outputs graphed represent averages of the number of days recorded in each instance.

the plasma. Thus, at the end of this mercurial diuretic period, the plasma sodium concentration had risen from 125 to 138 mEq. per liter. Figure 2 is a graphic representation of the patient's response to this regimen.

The patient was symptomatically strikingly improved, was edema free, and had a normal plasma electrolyte pattern. He was discharged from the hospital, and is at present being maintained edema-free on a regimen of salt and fluid restriction, daily ammonium chloride and bi-weekly mercurial injections.

The other 3 patients treated by this regimen showed similar clinical improvement, and rises in plasma sodium concentrations from 118–135 mEq., 119–128 mEq. and 122–136 mEq. per liter, respectively. These changes occurred in the course of a sustained diuresis resulting in each instance in a marked weight loss (14, 16, and 24 pounds respectively).

Discussion

The 2 cases reported above typify the group of cardiac patients that we have seen with fluid retention, hyponatremia, and hypochloremia. The positive water balance that we have found to be a consistent feature in these cases is clearly demonstrated. Treatment in this situation poses a difficult problem. In most instances, as in case 1, the administration of hypertonic saline solution in an attempt to correct the hyponatremia does not improve the clinical status of these patients. It often results in a further weight gain and a progression of already distressing symptoms.

A responsiveness to mercurial diuretics was restored by using Diamox and ammonium chloride to produce that rise in plasma chloride concentration necessary to provide for the presentation of an adequate chloride load to the renal tubules. Our empiric observation has been that this state is achieved when the urinary chloride concentration has risen to over 40 mEq. per liter. The mechanism of the action of Diamox in producing a rise in plasma chloride concentration has been studied.[9]

The significant characteristic of the mercurial-induced diuresis that occurred, once the necessary hyperchloremia has been achieved, was that each liter of urine had a considerably lower sodium content than the extracellular fluid. As a result, with fluid intake restricted, the sodium concentration of the extracellular

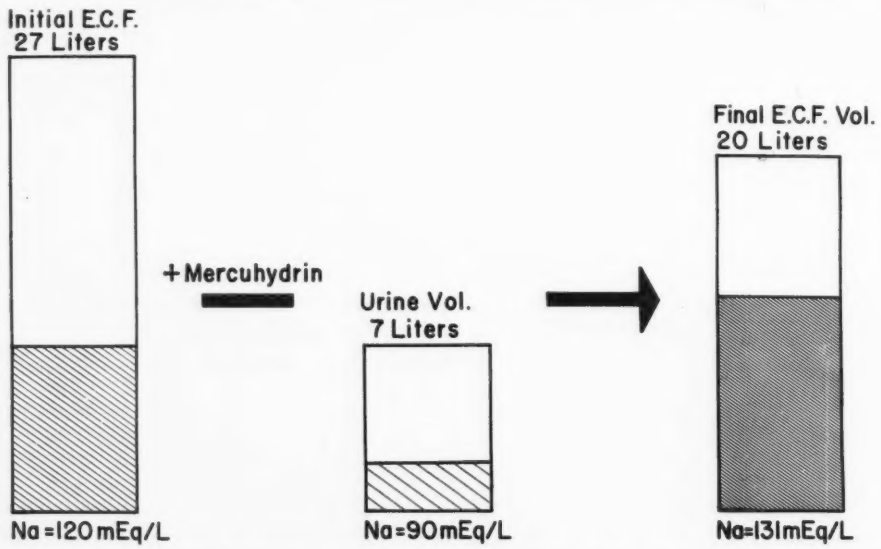

Fig. 3. Diagrammatic representation of the changes in extracellular fluid volume and sodium concentration that occur as a result of the diuresis achieved in the setting of a hyperchloremic acidosis by the application of the regimen described in the text.

Sodium 'gain' by body as a result of diuresis of a urine that is hypotonic for sodium with respect to the E.C.F. can be calculated as: [(120 (E.C.F. conc./L.) − 90 (urine conc./L.)] × 7 (liters of urine) = 210 mEq. of sodium available for redistribution in the E.C.F. remaining after diuresis.

fluid rose toward normal (fig. 3). Striking clinical improvement occurred in association with the diuresis and the return to normal of the plasma sodium concentration.

Producing an acidosis in an already azotemic patient is potentially hazardous, and the necessity for continued close clinical and laboratory observations cannot be overemphasized. However, with such observations, the acidosis has been without ill effect. The degree of acidosis and rise in plasma chloride concentration necessary to restore a responsiveness to mercurial diuretics varies with each individual patient. The essential indication that the necessary acidotic state has been achieved is a rise in urinary chloride concentration. It is to be emphasized that this is unrelated to a specific level of plasma pH or plasma chloride concentration. This principle is clearly demonstrated in the 2 cases reported above. In case 1, the urinary chloride concentration, initially 12.8 mEq. per liter, rose to 43 mEq. per liter when the plasma pH was 7.27 and the plasma chloride concentration was 114 mEq. per liter. By contrast, in case 2 the urine chloride concentration initially 2.8 mEq. per liter rose to 78.4 mEq. per liter (indicative of an adequate setting for mercurial administration) when the plasma pH was 7.34 and the plasma chloride concentration was only 102 mEq. per liter.

The effectiveness of this therapeutic approach, directed primarily toward reducing the expanded extracellular fluid volume, and not primarily toward increasing the sodium content of the extracellular fluid, supports the postulation that the mechanism for development of this syndrome is primarily fluid retention with extracellular fluid expansion, and not salt depletion. In keeping with this view is the role that mercurial diuretics play in the success of this regimen, when heretofore they have been purported to be a significant causative factor in producing the "low-salt" syndrome.

Conclusions

1. An effective regimen for treatment of the "low-salt syndrome" utilizing Diamox, ammonium chloride, and mercurial diuretics has been presented.

2. It is suggested that extracellular fluid expansion with electrolyte dilution is the major factor in the production of the "low-salt syndrome," which might more aptly be termed the "dilution syndrome."

Acknowledgment

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Summario in Interlingua

1. Es presentate un efficace regime pro le tractamento del "syndrome de basse nivellos de sal," utilisante Diamox, chlorido de ammonium, e diureticos mercurial.

2. Nos opina que le expansion extracellular de fluido occurrente in le presentia de dilution electrolytic es le major factor in le production del "syndrome a basse nivellos de sal." Il esserea plus appropriate designar iste syndrome como "syndrome de dilution."

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The Effects of Intravenous Apresoline (Hydralazine) on Cardiovascular and Renal Function in Patients with and without Congestive Heart Failure

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Intravenous Apresoline is a powerful renal vasodilator in cardiac as well as in noncardiac patients. In hypertensive patients in congestive heart failure, the drug produces a striking improvement in both cardiovascular and renal function. The increases in renal plasma flow are inconsistently related to changes in arterial pressure and cardiac output. Unlike many hypotensive drugs, Apresoline usually causes no decrease in the renal excretion of sodium and water. Circulatory collapse produced by the drug may occur in the presence of an increased cardiac output but is accompanied by a deterioration of the arterial pressure pulse and a reduction in sodium and water excretion.

PREVIOUS REPORTS[1-3] have shown that the acute administration of hydralazine* (Apresoline), a hypotensive agent, produces marked increases in renal blood flow in normal man as well as in patients with compensated hypertensive disease. Wilkinson and co-workers[3] have measured cardiovascular and renal hemodynamic function (but not simultaneously) in normal and hypertensive patients, and found that the acute administration of Apresoline increases not only the renal blood flow but also the cardiac output. These hemodynamic responses are strikingly different from those caused by other hypotensive agents such as dihydroergocornine (DHO), veratrum, and hexamethonium which in compensated hypertensive patients usually decrease (at least transiently) the renal blood flow and the sodium and water excretion without appreciably changing the cardiac output. To determine whether a fall in arterial pressure when associated with a *rise* in cardiac output and renal plasma flow might be accompanied by a rise in sodium and water excretion, it was decided to study the effect of intravenous Apresoline on electrolyte and water excretion as well as on cardiovascular and renal hemodynamic function.

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* Ciba Pharmaceutical Products, Inc. generously supplied the authors with hydralazine under the trade name Apresoline.

PATIENTS

Twelve patients with essential hypertension without heart failure were studied; eight with normal hearts and four with hypertensive heart disease. Thoracolumbar sympathectomy had been previously performed in two of these patients (V. V., S. O.). Ten patients were studied with valvular or nonvalvular heart disease and pulmonary hypertension including three (A. A., S. E., I. G.) with hypertensive cardiovascular disease and severe congestive failure and marked peripheral edema. Five had rheumatic heart disease with mitral stenosis or insufficiency without peripheral edema, and two (L. N., O. I.) had right ventricular failure as indicated by elevation of the right ventricular end diastolic pressure. Four patients had chronic pulmonary disease (emphysema) with mild to moderate pulmonary hypertension, but no peripheral edema or other clinical signs of right heart failure.

None of the compensated hypertensive patients had been on a low sodium diet or antihypertensive drug therapy for at least three months prior to the study. In addition, none of the patients with hypertensive cardiovascular disease in congestive heart

failure had been treated prior to the study with digitalis or diuretics. The two patients (O. I., L. N.) with atrial fibrillation were taking digitalis daily and were on a restricted sodium diet. Patient L. U. was also on a low sodium diet. With the exception of patient D. E. whose dietary intake of sodium had been limited, none of the patients with chronic lung disease were on specific cardiac therapy.

Methods

The patients were studied in the postabsorptive state without sedative medication. The cardiovascular and renal functions were measured by methods previously described.[4]

After preliminary practice of the procedure, one or two resting cardiac output determinations were made by the direct Fick method. During the periods prior to the administration of Apresoline, designated as the "control period," three to four 10 to 15 minute urine collections were obtained. The patients were then given Apresoline intravenously, either by rapid single injection or, in a few cases, more slowly at the rate of about 1 mg. per minute, in a dosage range of 14 to 50 mg. Measurements of brachial arterial, pulmonary arterial, and right ventricular pressures were made and repeated at three-minute intervals following the administration of the drug until the completion of the study. The determination of the cardiac output was made after the administration of Apresoline when there was an appreciable fall in the arterial pressure, which occurred 12 to 50 minutes from the start of the injection. During the period of injection of Apresoline, designated as "during Apresoline," urine collections were made at least at 10-minute intervals. Following the administration of the drug ("post-Apresoline period"), three or more urine collections were obtained at 10 to 20 minute intervals.

Results

The individual cardiovascular and renal data before and following the intravenous administration of Apresoline and the averages are presented in tables 1 and 2.

Cardiovascular Responses

Cardiac Index and Oxygen Measurements

Following the intravenous administration of Apresoline, four of the five patients with compensated hypertensive disease had an increase in cardiac index ranging from 0.86 to 1.85 L./M.^{2} body surface area, while one (S.O.) had no change. The average increase in cardiac index for the group was 1.10 L./min./M.^{2} or 28 per cent. The decompensated group of patients with mitral valvular disease had smaller rises in the cardiac index, the average increase being only 0.48 L./min./M.^{2} or 16 per cent. However, two patients (A. A., S. E.) with hypertensive cardiovascular disease and severe congestive heart failure had marked increases in the cardiac indices of 1.40 and 3.22 L./min./M.^{2} respectively (fig. 1). Since in these two cases the changes were not associated with increases in the heart rate as occurred in others, the rises in cardiac output were due solely to a greater stroke volume. The average increase in cardiac index in the group with chronic lung disease was comparable to that of the compensated hypertensive group.

Of four patients (O. O., L. M., L. U., L. O.) who developed circulatory collapse after the administration of intravenous Apresoline three had "tight" mitral stenosis and one had compensated hypertensive cardiovascular disease. During the state of vascular collapse three of the four patients had increased cardiac indices (fig. 2). In patient L. O. the determination of cardiac output was made before the development of collapse.

Since the changes in oxygen consumption were slight, the increases in cardiac output in the different groups were associated with a narrowing of the arteriovenous oxygen differences. The most striking decrease in the arteriovenous oxygen difference (8.36 volumes per 100 ml.) occurred in patient S. E. who had hypertensive cardiovascular disease and severe congestive heart failure.

Vascular Pressures

Pulmonary Arterial Pressure. In the hypertensive patients without heart failure, the mean pulmonary arterial pressure increased slightly or not at all after intravenous Apresoline, the average rise being 2 mm. Hg. In the group with cardiac insufficiency the changes in pulmonary arterial pressure, although definite in different cases, were inconsistent. In the patients with hypertensive cardiovascular disease and congestive heart failure (A. A., S. E.) reductions of 5 and 17 mm. Hg occurred in the mean pulmonary arterial pressure. These decreases were associated with marked increases in cardiac output. In contrast, patients with valvular heart disease, including those who

TABLE 1.—*Individual Cardiodynamic Data*

Patient, Age, Sex	Diagnosis and Clinical Classification	Procedure	Cardiac Index *L./min./M.²*	Stroke Index *ml./min./M.²*	Oxygen Consumption *ml./min./M²*	A-V Oxygen Difference *vol. %*	Pressures *mm. Hg*							Pulse Rate *beats/min.*	Resistances *Dynes/seconds/cm.⁻⁵*	
							Pulmonary artery			Right ventricular end diastolic	Systemic arterial				Total peripheral	Total pulmonary
							S	D	M		S	D	M			
Compensated Hypertensive Group																
O. O.*, 35, F	Ess. hyp.	Control	4.02	48	136	3.40	24	12	17	4	150	80	105	84	1310	210
			4.00	48	123	3.07	24	12	17	4	150	80	105	84	1320	210
		Post Apresoline (16 mg. I.V.)	4.87	44	131	2.69	34	18	24	6	100	55	70	110	720	250
H. S., 26, F	Ess. hyp.	Control	3.86	51	161	4.19	17	10	13	3	200	120	145	76	1850	170
		Post Apresoline (20 mg. I.V.)	5.71	55	159	2.79	25	14	18	1	190	105	135	104	1170	160
R. R., 34, M	H.C.V.D.I.	Control	3.83	62	170	4.44	23	12	15	4	250	125	165	62	1850	150
		Post Apresoline (30 mg. I.V.)	5.47	66	185	3.38	27	15	18	4	240	120	160	82	1120	130
K. B., 34, M	Ess. hyp.	Control	3.90	49	165	4.24	25	15	20	3	185	110	135	80	1420	210
			4.10	51	158	3.85	25	15	20	3	185	110	135	80	1360	200
		Post Apresoline (20 mg. I.V.)	—	—	—	—	25	15	20	3	150	80	105	96	—	—
F. D., 45, F	Ess. hyp.	Control	3.17	44	135	4.27	25	12	17	5	185	100	130	72	2280	300
			3.10	44	141	4.54	27	12	18	5	180	100	130	70	2330	320
		Post Apresoline (16 mg. I.V.)	4.45	49	135	3.04	25	12	17	2	140	80	100	92	1250	210
S. O., 40, M	H.C.V.D., I	Control	4.93	68	182	3.69	30	17	22	2	220	120	155	72	1280	180
		Post Apresoline (50 mg. I.V.)	4.82	63	167	3.47	37	18	24	1	220	110	145	76	1230	200
	Average	Control	3.96	55	156	3.99	24	13	18	4	198	109	139	74	1720	200
		Post Apresoline	5.06	55	155	3.07	29	15	20	3	173	92	119	93	1100	190
Cardiac Insufficiency Group																
A. A., 54, M	H.C.V.D., IV	Control	2.22	25	171	7.74	85	50	60	25	185	110	135	88	2560	1140
		Post Apresoline (20 mg. I.V.)	3.62	45	185	5.11	80	45	55	22	180	90	120	80	1390	640
S. E., 38, M	H.C.V.D., IV	Control	1.44	13	176	12.17	70	50	55	30	220	160	180	108	6040	1850
		Post Apresoline (50 mg. I.V.)	4.66	43	177	3.81	58	32	38	20	210	120	150	108	1560	390
I. G., 63, M	H.C.V.D., A.S.H.D., IV	Control	—	—	—	—	110	60	80	30	180	100	125	80	—	—
		Post Apresoline (20 mg. I.V.)	—	—	—	—	—	—	—	25	160	80	105	80	—	—
L. N., 50, M	R.H.D., M.I., A.F., III	Control	1.99	23	143	7.16	40	26	30	12	160	90	115	88	2390	620
		Post Apresoline (15 mg. I.V.)	2.48	24	150	6.04	40	26	30	12	130	70	90	105	1500	500
O. I., 38, M	R.H.D., M.I., A.F., IV	Control	1.66	19	143	8.62	50	32	36	14	110	80	90	88	2560	1020
			1.53	17	135	8.80	50	32	36	14	110	80	90	88	2790	1110
		Post Apresoline (25 mg. I.V.)	1.86	16	172	9.28	60	35	42	17	120	70	85	116	2160	1070
L. U.*, 23, F	R.H.D., M.S., III	Control	3.32	54	152	4.59	45	20	30	1	105	60	75	62	1210	480
		Post Apresoline (25 mg. I.V.)	4.09	54	161	3.93	50	30	40	4	60	35	45	76	590	520
L. O.*, 40, M	R.H.D., M.S., III	Control	3.25	41	145	4.45	45	35	40	5	130	85	100	78	1170	470
		Post Apresoline (15 mg. I.V.)	3.57	38	168	4.70	50	36	42	12	110	70	85	94	900	450
L. M.*, 37, M	R.H.D., M.S., III	Control	4.16	50	170	4.13	50	28	38	4	120	60	80	84	900	430
		Post Apresoline (18 mg. I.V.)	5.14	58	178	3.46	60	34	43	8	95	40	60	88	550	390
	Average	Control	2.57	32	157	6.99	55	34	41	15	151	93	113	85	2420	870
		Post Apresoline	3.63	40	170	5.19	57	34	41	15	133	72	93	93	1240	570

TABLE 1—*Continued*

Patient, Age, Sex	Diagnosis and Clinical Classification	Procedure	Cardiac Index *L./min./M.²*	Stroke Index *ml./min./M.²*	Oxygen Consumption *ml./min./M.²*	A-V Oxygen Difference *vol. %*	Pressures *mm. Hg*							Pulse Rate *beats/min.*	Resistances *Dynes/seconds/cm.⁻⁵*	
							Pulmonary artery			Right ventricular end diastolic	Systemic arterial				Total peripheral	"Total pulmonary"
							S	D	M		S	D	M			
Chronic Lung Disease Group																
G. M., 69, F	P.E.	Control	2.96	36	133	4.50	33	18	25	5	125	60	80	82	1300	410
			2.63	31	128	4.86	33	18	25	5	130	70	90	84	1650	460
		Post Apresoline (20 mg. I.V.)	4.50	45	154	3.43	45	24	32	9	90	60	70	100	750	340
D. E., 63, M	P.E., C.P.	Control	3.39	56	140	4.13	40	25	28	4	130	65	85	60	1080	360
		Post Apresoline (20 mg. I.V.)	3.45	57	143	4.14	45	28	33	5	110	55	75	60	940	410
A. E., 50, M	P.E., C.P.	Control	3.84	47	172	4.55	40	24	28	5	160	100	120	82	1340	310
		Post Apresoline (20 mg. I.V.)	5.58	61	193	3.46	45	28	33	7	140	80	100	92	770	260
M. O., 34, M	P.E., C.P.	Control	3.05	—	154	5.06	53	30	38	7	130	90	105	92	1570	570
		Post Apresoline (40 mg. I.V.)	—	—	—	—	67	38	48	9	130	80	95	116	—	—
	Average	Control	3.34	46	148	4.45	42	24	30	5	137	80	99	79	1300	360
		Post Apresoline	4.51	54	163	3.68	51	30	37	7	118	69	85	92	820	340

Ess. hyp. = Essential Hypertension; H.C.V.D. = hypertensive cardiovascular disease; A.S.H.D. = arteriosclerotic heart disease; A.F. = atrial fibrillation; R.H.D. = rheumatic heart disease; M.I. = mitral insufficiency; M.S. = mitral stenosis; P.E. = pulmonary emphysema; C.P. = cor pulmonale; S = systolic; D = diastolic; M = mean; M^2 refers to square meters of body surface area.

* Circulatory collapse developed in these patients following intravenous Apresoline.

had vascular collapse, usually had increases in pulmonary arterial pressure associated with rises in cardiac output. Patients with chronic lung disease had similar rises in pulmonary arterial pressure, the average increase being 7 mm. Hg.

Right Ventricular End Diastolic Pressure. In the compensated hypertensive patients the changes in measured right ventricular end diastolic (R.V.D.) pressure were slight and inconsistent. However, in patients with mitral valvular heart disease, including those who had circulatory collapse (fig. 2), and in patients with chronic lung disease the right ventricular end diastolic pressure usually increased from 1 to 7 mm. Hg. In contrast, the hypertensive patients with congestive heart failure had appreciable decreases in the right ventricular end diastolic pressure ranging from 3 to 10 mm. Hg.

Arterial Pressure. The reductions in mean arterial pressure after intravenous Apresoline were comparable in both the compensated hypertensive and cardiac insufficiency groups. The fall in blood pressure, however, in patients with chronic lung disease was less impressive. The marked reductions in blood pressure in three patients (L. O., L. M., L. U.) with mitral stenosis and in one (O. O.) with compensated hypertensive disease were associated with circulatory collapse. During this hypotensive state the arterial pressure pulse was low and flat, and the reflected dicrotic wave had disappeared.

Heart Rate

After intravenous Apresoline, the heart rate increased to a comparable degree in all three groups with the exception of the hypertensive patients in congestive failure.

Vascular Resistances

In all except the two hypertensive patients with congestive failure, the average change in the "total pulmonary" resistance was slight. However, in these two patients the "total pulmonary" resistance decreased markedly.

With the reduction in the arterial pressure and associated increase in cardiac output in the different groups the total peripheral resistance fell appreciably. The most striking reduction

TABLE 2.—*Individual Renal Data*

Patient, Age, Sex	Diagnosis and Clinical Classification	Procedure	C_{PAH} *ml./min./1.73 M²*	C_{IN} *ml./min./1.73 M²*	UV *ml./min.*	$U_{N_a}V$ *micro Eq./min.*	U_KV *micro Eq./min.*	Systemic Arterial Pressure *mm. Hg* S	D	M	Pulse Rate *beats/min.*
Compensated Hypertensive Group											
O. O.*, 35, F	Ess. hyp.	Control	340	92	5.9	1127	84	150	80	105	84
		During Apresoline (16 mg; I. V.)	382	83	5.0	939	70	100	55	70	110
		Post Apresoline	—	—	1.1	204	85	60	20	35	72
H. S., 26, F	Ess. hyp.	Control	587	162	12.2	101	83	200	120	145	76
		Post Apresoline (20 mg. I. V.)	686	168	4.7	88	118	190	105	135	104
R. R., 34, M	H.C.V.D., I	Control	564	132	10.0	179	152	250	125	165	62
		Post Apresoline (30 mg. I. V.)	827	126	10.0	170	150	240	120	160	82
K. B., 34, M	Ess. hyp.	Control	757	139	8.7	169	148	185	110	135	80
		Post Apresoline (20 mg. I. V.)	955	152	9.0	181	266	150	80	105	96
F. D., 45, F	Ess. hyp.	Control	469	97	7.8	149	91	180	100	130	70
		Post Apresoline (16 mg. I. V.)	576	92	5.0	102	79	140	80	100	92
S. O., 40, M	H.C.V.D., I	Control	431	124	4.5	457	124	220	120	155	72
		Post Apresoline (50 mg. I. V.)	476	135	4.0	418	111	220	110	145	76
R. O'D., 52, M	H.C.V.D., I	Control	323	78	3.2	457	112	200	110	140	66
		During Apresoline (50 mg. I. V.)	448	83	5.3	538	149	200	80	120	74
		Post Apresoline	549	80	5.0	438	109	180	80	115	82
E. H., 39, F	H.C.V.D., I	Control	—	—	9.4	732	81	210	110	145	74
		During Apresoline (40 mg. I. V.)	—	—	15.6	820	78	180	75	110	110
		Post Apresoline	—	—	11.2	740	86	130	60	85	100
G. C., 49, F	H.C.V.D., I	Control	459	107	8.0	1176	118	190	100	130	80
		Post Apresoline (20 mg. I. V.)	765	128	5.3	1100	148	190	100	130	120
V. V., 36, F	Ess. hyp.	Control	675	129	5.5	100	74	145	80	100	72
		Post Apresoline (12.5 mg. I. V.)	811	143	7.3	139	99	130	70	90	94
		Average control	512	118	8.3	422	117	193	106	135	74
		Average post Apresoline	693	123	6.3	358	125	163	82	110	92
Cardiac Insufficiency Group											
A. A., 54, M	H.C.V.D., IV	Control	241	91	4.7	85	60	185	110	135	88
		Post Apresoline (20 mg. I. V.)	440	120	8.2	762	156	180	90	120	80
S. E., 38, M	H.C.V.D., IV	Control	164	107	1.4	9	21	220	160	180	108
		During Apresoline (50 mg. I. V.)	238	127	10.2	469	91	210	120	150	108
		Post Apresoline	330	150	10.6	835	—	210	120	150	108
I. G., 63, M	H.C.V.D., A.S.H.D., IV	Control	154	84	0.6	40	54	180	100	125	80
		During Apresoline (20 mg. IV.)	162	76	0.5	104	64	160	80	105	80
		Post Apresoline	302	100	2.3	389	114	140	70	95	76

TABLE 2.—*Continued*

Patient, Age, Sex	Diagnosis and Clinical Classification	Procedure	C_{PAH} *ml./min./ 1.73 M²*	C_{IN} *ml./min./ 1.73 M²*	UV *ml./ min.*	$U_{Na}V$ *micro Eq./ min.*	U_KV *micro Eq./min.*	Systemic Arterial Pressure *mm. Hg* S	D	M	Pulse Rate *beats/ min.*
		Cadiac Insufficiency Group—*Continued*									
L. N., 50, M	R.H.D., M.I., A.F., III	Control	246	105	0.9	24	53	160	90	115	88
		Post Apresoline (15 mg. I.V.)	294	103	1.0	25	58	130	70	90	105
O. I., 38, M	R.H.D., M.I., A.F., IV	Control	200	86	0.6	120	58	110	80	90	88
		Post Apresoline (15 mg. I.V.)	273	97	0.7	153	96	120	70	85	116
L. U.*, 23, F	R.H.D., M.S., IV	Control	391	115	0.4	28	37	105	60	75	62
		Post Apresoline (25 mg. I.V.)	433	137	0.4	36	43	60	35	45	76
L. O.*, 40, M	R.H.D., M.S., III	Control	198	69	1.0	221	56	130	85	100	78
		During Apresoline (15 mg. I.V.)	326	108	2.2	496	115	110	70	85	94
		Post Apresoline	219	75	0.7	106	78	60	30	40	84
L. M.*, 37, M	R.H.D., M.S., III	Control	454	126	2.0	549	92	120	60	80	84
		During Apresoline (18 mg. I.V.)	604	153	2.7	527	187	105	50	70	82
		Post Apresoline	502	99	0.8	103	142	95	40	60	88
		Average control	256	98	1.4	134	54	151	93	112	84
		Average during Apresoline	332	116	3.9	399	114	146	80	102	91
		Average post Apresoline	349	110	3.1	301	98	124	66	86	92
		Chronic Lung Disease Group									
G. M., 69, F	P.E.	Control	212	52	2.1	270	52	130	65	85	83
		Post Apresoline (20 mg. I.V.)	292	58	1.7	279	72	90	60	70	100
D. E., 63, M	P.E., C.P.	Control	359	—	0.5	25	36	130	65	85	60
		Post Apresoline (20 mg. I.V.)	440	—	0.4	36	39	110	55	75	60
A. E., 50, M	P.E., C.P.	Control	442	116	0.9	143	81	150	90	110	86
		Post Apresoline (20 mg. I.V.)	559	123	0.7	103	61	140	80	100	92
M. O., 34, M	P.E., C.P.	Control	189	76	2.9	195	100	130	90	105	92
		Post Apresoline (40 mg. I.V.)	295	99	3.5	256	193	130	80	95	116
		Average control	300	81	1.6	158	67	135	78	101	80
		Average post Apresoline	396	92	1.6	168	91	118	68	85	92

in the total peripheral resistance occurred in the hypertensive patients with congestive failure.

Renal Data

Para-aminohippurate (PAH) Clearance (Renal Plasma Flow)

Half the hypertensive group and all the cardiac and pulmonary insufficiency groups had a reduced control para-aminohippurate clearance. The average control PAH clearances in the latter groups were similar, but 40 to 50 per cent less than in the hypertensive group. Following intravenous Apresoline, all three groups had appreciable increases in renal plasma flow. The average increase in the compensated hypertensive group was 35 per cent; in the chronic pulmonary disease group,

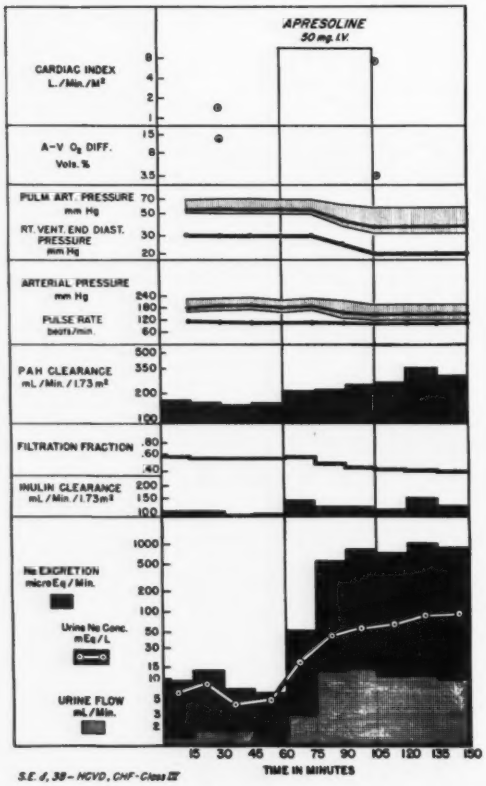

FIG. 1. Cardiovascular and renal responses to intravenous Apresoline in a hypertensive patient in congestive heart failure. Note the marked increases in the excretion of sodium and water associated with the decrease in the arterial pressure and the increases in cardiac output, renal plasma flow, and glomerular filtration rate.

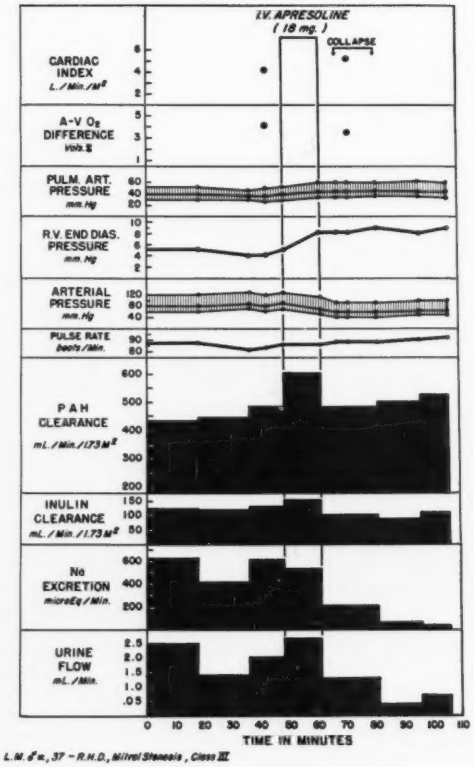

FIG. 2. Cardiovascular and renal responses to Apresoline-induced collapse in a patient with mitral stenosis. Note during vascular collapse the cardiac index is increased, the elevated pulmonary arterial and right ventricular end diastolic pressures are not altered, and renal plasma flow is maintained, but that the glomerular filtration rate and the excretion of sodium and water are decreased.

32 per cent; and in the cardiac insufficiency group, 36 per cent. The greatest percentage rise in the renal plasma flow occurred in hypertensive patients in congestive heart failure, the average increase being 92 per cent. In three patients with mitral stenosis (L. O., L. U., L. M.), who developed circulatory collapse, the measured renal plasma flow did not decrease below the value in the control period, but in two of the three patients it did fall below the level attained in the precollapse period after Apresoline (fig. 2).

Inulin Clearance (Glomerular Filtration Rate)

In the hypertensive group the average inulin clearance in the control period was 20 per cent higher than that in the cardiac group and 31 per cent higher than that in the chronic pulmonary disease group. In the latter two groups, this function was usually depressed whereas in the hypertensive group it not infrequently was within the normal range. Following intravenous Apresoline, the glomerular filtration rate increased slightly, but inconsistently in the hypertensive group. The increase, however, was both more consistent and more striking

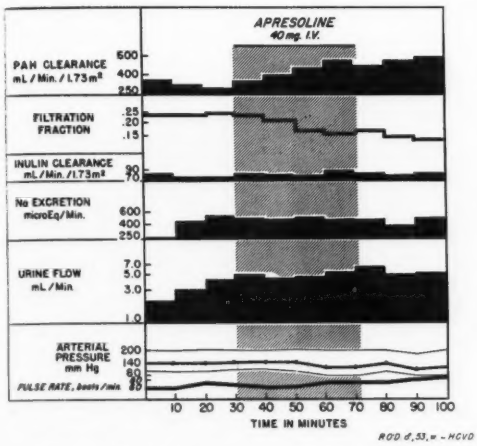

FIG. 3. Circulatory and renal responses to intravenous Apresoline in a patient with essential hypertension.

in the cardiac group. The hypertensive patients with heart failure tended to have the greatest increase in glomerular filtration rate. The average maximal rise in glomerular filtration rate in the compensated hypertensive group was 4 per cent and in the cardiac insufficiency group was 23 per cent. Only one patient (M. O.) in the group with chronic pulmonary disease had an appreciable change in glomerular filtration rate. In all groups of patients the increase in renal plasma flow was greater than the increase in glomerular filtration rate.

In the three patients with mitral stenosis who developed vascular collapse the glomerular filtration rate usually fell below the previous high (post-Apresoline) level, but not below the control (pre-Apresoline) value with the exception of patient L. M.

Electrolyte and Water Excretion

The control sodium and water excretion in the hypertensive group (without heart failure) was considerably higher than the control values in the cardiac and chronic pulmonary disease groups. Following intravenous Apresoline the changes in sodium and water excretion in the hypertensive group, with the exception of patient O. O., were slight and inconsistent (fig. 3). The average change in the group was negligible.

In contrast, the sodium and water excretion in the cardiac insufficiency group usually increased. The most impressive increases in sodium and water excretion in this group occurred in hypertensive patients in congestive heart failure and were associated with appreciable increases in glomerular filtration rate and renal plasma flow (fig. 1). The increase in sodium excretion in these patients ranged from 349 to 826 microequivalents per minute.

The excretion of sodium and water after intravenous Apresoline was strikingly reduced in the patients who developed circulatory collapse, with the exception of patient L. U. in whom the excretion of sodium and water was very low even during the control period. In patient L. O., although the sodium and water excretion fell below the control level, the glomerular filtration rate did not.

In general, potassium excretion varied in the same direction as did the glomerular filtration rate. The average increase in potassium excretion in the hypertensive group without heart failure was 7 per cent; in the cardiac insufficiency group, 81 per cent; and in the chronic lung disease group, 36 per cent.

The Effects of Intravenous Apresoline during Acute Reductions in Renal Excretion of Sodium and Water

Since it appeared that intravenous Apresoline caused marked increases in sodium, potassium, and water excretion in decompensated hypertensive patients who were chronically retaining sodium and water as manifested by peripheral edema, it seemed possible that this drug might prevent or correct acute reductions in salt and water excretions such as may be produced by cuff congestion of the limbs or intravenous injection of hexamethonium. Its effect during acute renal retention of sodium and water was therefore studied in four compensated hypertensive patients. In three of these patients (S. O., R. O'D., M. R.) a reduction in sodium and water excretion had been induced by decreasing the effective blood volume with congesting cuffs on the thighs. The cuffs were

TABLE 3.—*The Effects of Intravenous Apresoline During Acutely Induced Reductions in Sodium and Water Excretion*

Patient, Age, Sex	Procedure	Period	Duration min.	C_{HPA} ml./min./1.73 M^2	C_{IN} ml./min./1.73 M^2	UV ml./min.	$U_{Na}V$ microEq./min.	Arterial Pressure, S/D (M) mm. Hg	Pulse Rate beats/min.	Cardiac Index L./min./M^2
S. O., 40; M	Control	1–4	49	431	124	4.5	457	220/120 (155)	72	4.93
	Apresoline (50 mg.)	5–7	54	476	135	4.0	418	220/110 (145)	76	4.82
	Congestion*	8–10	56	472	121	1.6	184	200/100 (135)	70	4.10
	Recovery	11	10	516	132	0.8	59	220/110 (155)	72	—
R. O'D., 52, M	Control	1–4	47	331	84	5.4	556	200/115 (140)	60	—
	Congestion	5–9	57	282	80	3.9	337	185/110 (135)	68	—
	Congestion & Apresoline (40 mg.)	10–16	77	397	75	0.8	139	150/80 (105)	82	—
	Recovery	17–18	23	—	—	1.3	228	160/90 (110)	88	—
M. R., 44, F	Control	1–3	28	563	117	3.1	140	180/90 (120)	100	5.19
	Congestion	4–5	24	421	92	4.0	136	160/100 (120)	112	3.48
	Congestion & Apresoline (20 mg.)	6–8	47	397	90	1.0	95	120/70 (90)	115	—
	Recovery	9–10	29	714	88	0.4	57	120/70 (90)	105	—
L. A., 40, F	Control	1–3	40	322	—	3.4	162	220/120 (170)	80	3.79
	C_6 (6 mg.)	4–5	31	289	—	0.8	25	160/100 (125)	80	3.76
	Apresoline	6–8	38	323	—	0.5	9	120/75 (95)	82	4.35

C_6 = Hexamethonium.

* Period during which cuffs on thigh were inflated to 70 mm. Hg.

inflated to a pressure of 70 mm. Hg for at least one hour. The results of the experiment (table 3) indicate that irrespective of whether Apresoline was given before or after the cuff congestion, it did not prevent or noticeably counteract the reduction in sodium and water excretion. The inability of intravenous Apresoline to increase sodium and water excretion during venous congestion was found to be associated with a failure to increase appreciably the glomerular filtration rate and cardiac output at the same time.

In patient L. A., a decrease in renal excretion of sodium and water had been produced with intravenous hexamethonium. In this experiment, the administration of Apresoline likewise failed to augment sodium and water excretion. Slight increases in renal plasma flow (glomerular filtration rate not being measured) and cardiac output were associated with this response.

DISCUSSION

The cardiovascular and renal hemodynamic changes produced by intravenous Apresoline in individuals without heart failure are similar to those reported by previous investigators.[1-3] Intravenous Apresoline was also found to increase cardiac output and renal plasma flow in patients with cardiac insufficiency or with chronic pulmonary disease. The relationship between increases in renal plasma flow and changes in cardiac output and arterial pressure were inconsistent. This finding suggests an independent action of Apresoline on the kidney as well as on the heart and does not necessarily exclude the possibility that the resulting changes in cardiac output and arterial pressure also affected renal plasma flow. The vasodilating effect of Apresoline on the kidneys appears to be related to the pre-existing degree of renal vasoconstriction since those patients who had the lowest initial renal plasma flows tended to have the largest increases following the administration of intravenous Apresoline. An additional augmentation of renal plasma flow secondary to a rise in cardiac output is suggested by the response of hypertensive patients in heart failure who had the largest

increases both in renal plasma flow and cardiac output.

Patients with valvular heart disease tended to have smaller increases in cardiac output after Apresoline than patients without this disorder. It seems probable that greater increases in cardiac output did not occur in these patients mainly because of the mechanical disturbance in blood flow through the heart caused by the damaged valves. A mechanical interference with flow may likewise explain in part the higher incidence of circulatory collapse in patients with mitral stenosis. It is possible that if blood flow through the stenotic mitral orifice had not been impeded, a larger increase in cardiac output might have helped to maintain the blood pressure and prevent collapse. The finding of an increased cardiac output during collapse after Apresoline indicates that a reduction in cardiac output does not necessarily signal this state. A marked reduction in arterial pressure associated with an advanced deterioration of the arterial pressure pulse may be a more reliable signal of circulatory collapse.

Unlike patients with valvular heart disease and chronic pulmonary disease, hypertensive patients in congestive heart failure had reductions in the pulmonary arterial and intracardiac pressures with the increase in cardiac output. It appears not unlikely that the former changes resulted from a more efficient emptying of the left ventricle, as suggested by a reduction in the "wedge" pressure or "pulmonary capillary" pressure in patient A. A. from 40 to 35 mm. Hg. The improved emptying and increase in left ventricular stroke output may primarily be dependent upon a lowering of the systemic arterial pressure and peripheral resistance. However, Apresoline might also have improved cardiac function by stimulating directly or indirectly the myocardium. The improvement in cardiovascular function in hypertensive patients in congestive heart failure has also been reported following the administration of other hypotensive drugs, such as hexamethonium (5) and veratrum (6).

Unlike many hypotensive agents such as veratrum, dihydroergocornine and hexamethonium, intravenous Apresoline usually caused no decrease in the renal excretion of sodium and water in compensated individuals. The maintenance of sodium and water excretion during a reduction in blood pressure suggests the possibility that acute changes in blood pressure per se do not regulate the excretion of sodium and water, but that an associated renal hemodynamic change or changes may regulate these functions. Sodium amytal[7] and reserpine[8] are two other hypotensive agents which reduce blood pressure without usually altering sodium and water excretion. They, like Apresoline, differ from hypotensive drugs which reduce sodium and water excretion in that they do not reduce the renal plasma flow.

Although a reduction in blood pressure per se may not be a stimulus for the renal retention of sodium and water, a critical reduction with associated collapse changes in the arterial pressure pulse may cause such responses. This possibility was suggested in three patients who had reductions in sodium and water excretions following a marked fall in arterial pressure and the development of a collapse type of arterial pressure pulse. Although other hemodynamic factors (cardiac output, pulmonary arterial and right ventricular pressures) may have operated to reduce sodium and water excretion in these patients, they were not identifiable from the hemodynamic measurements obtained. Apresoline had a pronounced effect on the renal excretion of sodium, potassium, and water in hypertensive patients in congestive heart failure. The increases in sodium excretion ranged from 349 to 826 microequivalents per minute and were associated with both an improvement in cardiovascular and renal hemodynamic function. The increases in glomerular filtration rate were of such magnitude that they alone could account for the striking increases in the electrolyte and water excretion. Although alterations in renal tubular function might likewise have contributed to these changes, there was no evidence in the cuff congestion experiments to suggest that Apresoline interfered with the renal tubular reabsorption of sodium and water. It is possible that the striking improvement in renal function and increase in the excretion of electrolytes and water in hypertensive patients in congestive heart failure may be produced not

only by Apresoline but by other hypotensive agents which increase cardiac output.

Conclusions

(1) Intravenous Apresoline is a potent renal vasodilator in patients with cardiac insufficiency and in patients with chronic lung disease as well as in compensated hypertensive patients. The renal responses do not necessarily depend upon changes in cardiac output and arterial pressure.

(2) Intravenous Apresoline produces the most striking improvement in cardiovascular and renal function in hypertensive patients in congestive heart failure.

(3) The hypotensive effect of Apresoline, unless associated with circulatory collapse, is not accompanied by decreases in sodium and water excretion.

(4) Apresoline-induced vascular collapse frequently occurs in the presence of an increased cardiac output and appears primarily related to a marked reduction in blood pressure and to the deterioration of the arterial pressure pulse.

Summario in Interlingua

Apresolina intravenose es un potente vasodilatator renal in patientes cardiac e etiam noncardiac. In patientes hypertensive in congestive disfallimento cardiac, le droga produce un frappante melioration del functionamento e cardiovascular e renal. Le augmentos del fluxo de plasma renal es irregularmente relationate con alterationes de pression arterial e de volumine cardiac. In contrasto con multe drogas hypotensive, Apresolina non causa usualmente un reduction del excretion renal de natrium e aqua. Collapso circulatori causate per le droga pote occurrer in le presentia de augmentate volumine cardiac sed es accompaniate per un deterioration del pulso de pression arterial e un reduction del excretion de natrium e aqua.

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Plasma Lipids and Proteins and their Relationship to Coronary Disease among Navajo Indians

By IRVINE H. PAGE, M.D., LENA A. LEWIS, PH.D., AND JARVEY GILBERT, M.D.

Coronary disease is rare among the Navajo Indians. Their plasma proteins and lipids differ from those of the population of Cleveland in that albumin is low normal and α- and γ-globulin elevated; total cholesterol was much lower. Since the diet and living habits are not strikingly different from those of the control group, it is suggested that heredity, in this case, is the most likely explanation for the low incidence of coronary disease and low level of cholesterol. Neither in the control nor Navajo group did mean serum total cholesterol rise with age.

REVIEW of the records of the Navajo Medical Center General Hospital at Fort Defiance, Arizona, showed that the diagnosis of myocardial infarction was made in only 5 full-blooded Navajo Indians among 10,267 admissions over a 4-year period.[1] Even in the 5, electrocardiographic evidence failed to confirm the diagnosis. During the same period there were 60,405 out-patient visits without a single patient showing evidence of coronary disease. For comparison, the records for the same period at St. Joseph's Hospital in Albuquerque, New Mexico, about 150 miles from the Navajo Medical Center, were reviewed. The number of admissions of white people was 20,289; of these, 146 had myocardial infarction. The distribution of the various age groups was about the same in both hospitals.

Navajos usually eat a typically American diet, often containing high-cholesterol and high-fat foods. They eat less fruit and vegetables and fry more of their foods than we do. They are well nourished; the average weight of 100 male out-patients over 30 years of age was 159 pounds (range 102 to 275 pounds) and average height 67.4 inches. The average of females weighed 147 pounds (range 101 to 220 pounds) and the average height was 62 inches. Noniodized salt is used abundantly; food is usually highly seasoned.

This striking lack of coronary disease among the Navajo people, while consuming the average American diet, prompted us to examine their plasma proteins and lipids. It is our belief that atherosclerosis is rarely caused by one defect alone, such as hyperlipemia; rather, it is the resultant of multiple factors such as diet, elevated plasma lipids, the quality of the blood vessels and the filtration pressure. This concept has recently been summarized by one of us.[2]

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METHODS

Lipoproteins were studied by Gofman's ultracentrifuge technic[3] as modified by Lewis, Green, and Page.[4] The designation of the unit of measurement $-S_{1.21}$ represents a negative sedimentation of 1×10^{-13} cm. per second per dyne per grams at a density of 1.21 and temperature of 26 C. The advantage of using the higher density is that it allows measurement of the α-lipoproteins.

Cholesterol was determined by the method of Abell, Levy, Brodie, and Kendall.[5] We are indebted to Dr. Helen Brown for these determinations. The electrophoretic analysis of serum proteins was by Longsworth's modification of the Tiselius technic, with phosphate buffer of pH 7.8 and ionic strength of 0.16 μ.

Blood samples were drawn from fasting patients hospitalized at the Navajo Medical Center, Fort Defiance, Ariz., with the variety of diseases ordinarily found in a general hospital. Those with diseases known to be associated with hyperlipemia were avoided. The serum samples were shipped by air in iced Thermos bottles to the Cleveland Clinic for analysis. All of the patients studied were full-blooded Navajos.

RESULTS

The number of examinations of the serum lipoproteins was not sufficiently great to justify

TABLE 1.—*Serum Proteins of Navajo Indians*

Group	No. and Sex of Subjects	Age (Mean ± S. E. of Mean)	Total Protein Gm./100 ml.	Albumin		α_1 and α_2 Globulin		β-Globulin		γ-Globulin	
				Gm./100 ml.	%	Gm./100 ml.	%	Gm./100 ml.	%	Gm./100 ml.	%
Younger group (17–39 yrs.)	15 (12 M 3 F)	31 ± 1.7	6.94 ± 0.36	3.53 ± 0.20	51.0 ± 1.5	0.70 ± 0.05	10.0 ± 0.56	1.20 ± 0.04	17.3 ± 0.56	1.49 ± 0.06	21.5 ± 1.00
Older group (42–85 yrs.)	21 (13 M 8 F)	59 ± 3.4	6.76 ± 0.25	3.28 ± 0.08	48.6 ± 1.0	0.68 ± 0.04	10.2 ± 0.54	1.24 ± 0.04	18.4 ± 0.54	1.53 ± 0.07	22.7 ± 1.09
Cleveland controls	27 (12 M 15 F)	29.5 ± 1.72	7.44 ± 0.15	4.74 ± 0.11	63.5 ± 1.09	0.54 ± 0.04	7.2 ± 0.36	1.11 ± 0.03	15.2 ± 0.40	1.04 ± 0.05	14.1 ± 0.56

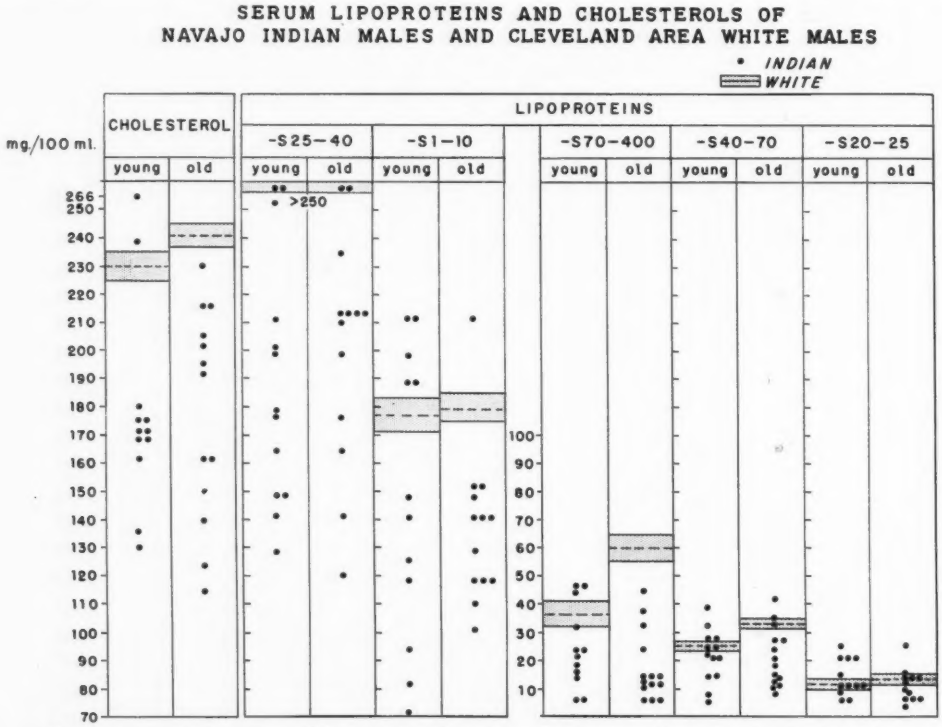

FIG. 1. Serum cholesterols and lipoproteins determined by ultracentrifugation, d 1.21, with sodium chloride and potassium bromide, of Navajo Indian males and Cleveland area white males. Shaded area represents Mean ± the standard error of the Mean, of normal white males from Cleveland.

separate analysis by sexes. Instead, subjects were divided into younger (31 years mean age) and older (59 years mean age).

The mean of the total plasma proteins of the Navajo Indians was only slightly lower than the average found in people from the Cleveland area; albumin was lower, 3.21–3.53 Gm. as compared with 4.74 in the Cleveland group (table 1 and figs. 1 and 2). Globulins tended to be slightly elevated, especially in the α- and

SERUM LIPOPROTEINS AND CHOLESTEROL OF NAVAJO INDIAN FEMALES AND CLEVELAND AREA WHITE FEMALES

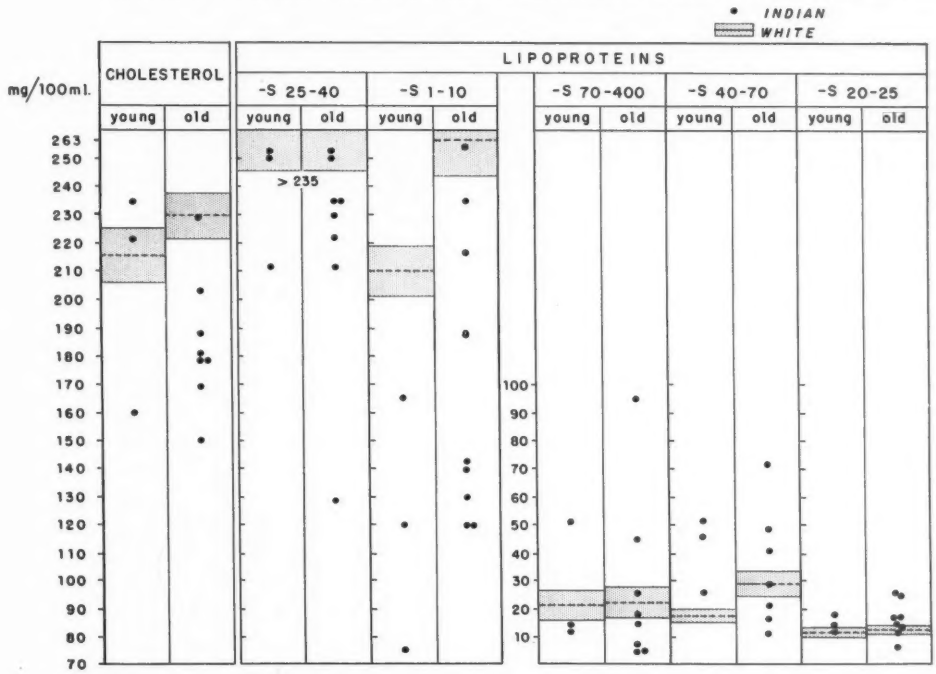

FIG. 2. Serum cholesterols and lipoproteins determined by ultracentrifugation, d 1.21, with sodium chloride and potassium bromide, of Navajo Indian females and Cleveland area white females.

TABLE 2.—*Serum Cholesterols and Lipoproteins of Navajo Indians*

	No. of Subjects	Age, Yr.	Lipoproteins mg./100 ml.					Cholesterol mg./100 ml.
			—S70–400	40–70	25–40	20–25	1–10	
Navajo Indians								
Young Men	12	32 ± 1.7*	25 ± 4.1	21 ± 2.8	199 ± 15.0	16 ± 2.0	148 ± 11.1	178 ± 11
Older Men	13	64 ± 3.3	15 ± 2.9	22 ± 3.2	205 ± 15.0	11 ± 1.3	140 ± 10.0	175 ± 10
Young Women	3	28†	37	42	235	18	142	189
		range 17–35	14–52	28–52	212–282	14–21	75–188	160–240
Older Women	8	54†	30	31	215	15	161	186
		range 42–85	7–96	14–49	146–260	7–26	87–260	150–229
Cleveland controls								
Young Men	58	27 ± 1.1	36.7 ± 3.8	24.2 ± 1.8	>250	11.6 ± 1.1	177.5 ± 5.9	230 ± 4.4
Older Men	99	45 ± 0.9	59.5 ± 5.0	32.7 ± 1.8	>250	12.4 ± 0.8	179.5 ± 5.5	242 ± 3.0
Young Women	42	26 ± 1.2	21.8 ± 4.3	18.1 ± 1.4	>235	11.6 ± 1.2	210.4 ± 9.7	216 ± 8.4
Older Women	25	43 ± 1.5	22.0 ± 5.0	29.1 ± 4.2	>235	13.3 ± 1.4	263.1 ± 13.5	230 ± 8.9

* Mean ± standard error of mean.

† S.E. not calculated because of insufficient numbers.

γ-fractions; the β-fraction was the same as in the Cleveland control group.

The various lipoprotein components of serum of the Indians were also very similar to those of our Cleveland control group. The $-S_{25-40}$ and $-S_{1-10}$ fractions tended to be lower in the Indians. These fractions correspond to β_1 and α_1 lipoprotein. Mean total cholesterol values were lower in the Indians by approximately 50 mg. per 100 ml. The analytic variation with the method employed was 4 mg. per 100 ml. in serum containing normal amounts of cholesterol. There was no difference between the older and younger age groups, either among the Indians or the control group (table 2 and figs. 1 and 2).

Discussion

There seems to be little doubt that coronary disease is uncommon among Navajo Indians. The plasma proteins of the Indians differ from those of a control group from the Cleveland area in having somewhat lower value for albumin. It would be idle to speculate on the cause because there are so many possibilities. The difference is not great enough to suspect widespread malnutrition among the Indians. The elevated γ-globulin may have been a characteristic of the Navajo population or may have reflected some rather widespread pathologic conditions. We have no way of knowing which is correct. The association of elevated γ-globulin levels and low serum cholesterol is reminiscent of our findings in patients with myelomatosis.[6] The only significant difference in the lipoprotein pattern is the slightly lowered α_1- and β_1-fractions. The supposedly most highly atherogenic fractions ($-S_{40-70}$ and $-S_{70-400}$) did not vary from values found in the controls.

Serum total cholesterol was definitely lower in the Indians and this may be one facet of the low degree of atherogenesis among the Navajo Indians. A difference in means of 50 mg. per 100 ml. appears sufficiently great to be of importance, although ignorance must be admitted about what differences are significant in terms of atherogenesis. In neither controls nor Indians was there a difference in the level of serum cholesterol between the younger and older groups. This confirms our observation on a smaller but very critically selected group of normal white persons.[7] We believe that serum cholesterol rises in some people with aging; whether as a result of disease or simply as normal accompaniment of aging is not known. Contrariwise, a rise does not occur under many other circumstances.

Since the Navajo diet as far as cholesterol intake is concerned is the same as that of most Americans, according to Gilbert,[1] it is hard to explain why the serum cholesterol levels are lower than levels of the non-Indian population living in the same geographic area. The Navajo people live to ages at which coronary artery disease develops in other people.

The most likely explanation for both the reduced levels of serum cholesterol and the low incidence of coronary disease seems to us to be heredity. As Gilbert puts it, "Navajos almost never become bald. They have practically no hair on the chest or the sides of the face. They are different outwardly, probably because of heredity, and probably are also different inwardly."

The importance of heredity in determining the serum cholesterol and lipoprotein pattern has been emphasized by studies on 2 strains of dwarf pigs, a long-lean and a short-fat type. The concentration of serum cholesterol and lower density (i.e. $-S_{70-400}$, $-S_{40-70}$ and $-S_{15-40}$) lipoproteins was significantly higher in the short-fat than the lean animals.[8]

Chavez[9] has shown that essential hypertension is rare among the poor Mexican and Indian population (2.6 per cent) and rises (37 per cent) among the pure white and those with little Indian blood. Angina pectoris, coronary thrombosis, and coronary atherosclerosis were also infrequent in the former group. Chavez writes me that the diet of the Indian population in Mexico is mostly carbohydrate; fat and protein intake is very low. The fat intake amounts to 12 to 14 per cent of the total caloric intake and protein to 10 to 12 per cent. It is interesting to compare these Indians with the Navajos in whom a diet high in fat apparently failed to increase the incidence of atherosclerosis. While such evidence as this is not conclusive, nevertheless it suggests caution in the accept-

ance of radical changes in diet calculated to prevent coronary atherosclerosis. On the other hand it should not engender a fatalistic attitude to close the door to human dietary experimentation.

Acknowledgment

We wish to express our deep appreciation to Dr. Marion Sumner for his help in collecting the blood samples. The technical assistance of Mrs. Laverne Fisher is gratefully acknowledged.

Summary

1. The serum cholesterol, proteins and lipoproteins have been measured in a group of pure-blooded Navajo Indians because of the observations that coronary artery disease among them is rare.

2. Comparison with plasma of a non-Indian population in the Cleveland area shows albumin to be low normal and α and γ-globulin elevated in the Indians. Alpha$_1$ and β_1-lipoproteins were low but the remainder of the lipoproteins did not differ from the controls. Mean total cholesterol was lower than that in the control group by a degree well outside the analytic error.

3. Since diet and living habits of the Navajos were not strikingly different from those of the control group, heredity seems the most likely explanation for both the low incidence of coronary disease and the low level of serum cholesterol. Probably contributing to the low incidence of coronary disease were the low plasma cholesterol levels.

4. In neither the control nor Navajo groups did mean serum total cholesterol rise with age.

Summario in Interlingua

1. Le cholesterol, proteinas, e lipoproteinas del sero esseva mesurate in un gruppo de indianos navajo de sanguine pur, proque il habeva essite observate que morbo de arteria coronari es rar in iste populo.

2. Le comparation con studios de plasma ab subjectos non-indian in le area de Cleveland monstrava que in le indianas le nivello de albumina es basse-normal durante que le globulinas α e γ ha nivellos elevate. Lipoproteinas α e β_1 monstrava nivellos basse, sed le altere lipoproteinas non differeva ab le valores del gruppo de controlo. Le valores median del cholesterol total esseva plus basse que in le gruppo de controlo. Le differentia excedeva le margine de error analytic.

3. Proque le dieta e le habitudes del viver inter le navajos non differeva frappantemente ab illos del gruppo de controlo, hereditate pare offerer le plus satisfacente explication del basse frequentia de morbo coronari e del basse nivello de cholesterol seral. Il es probabile que le basse nivellos de cholesterol plasmatic contribueva a reducer le frequentia de morbo coronari.

4. Le nivello median de cholesterol total del sero non se augmentava con le etate del subjectos in o le gruppo de controlo o le gruppo del navajos.

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Clinical and Hemodynamic Studies of Tricuspid Stenosis

By PAUL N. YU, M.D., DWIGHT E. HARKEN, M.D., FRANK W. LOVEJOY, JR., M.D., ROBERT E. NYE, JR., M.D., AND EARLE B. MAHONEY, M.D.

Five patients with tricuspid stenosis accompanying mitral stenosis were studied. The characteristic features include a diastolic rumbling murmur in the tricuspid area, accentuated by inspiration, prominent "a" wave in the jugular pulse, prominent P wave in the electrocardiogram, absence of physical or electrocardiographic signs of right ventricular hypertrophy, and disproportionate right atrial enlargement by fluoroscopy. The diagnosis may be confirmed by the presence of a significant diastolic pressure gradient across the tricuspid valve. Mitral valvuloplasty alone produces no improvement. The concept of "functional tricuspid stenosis" is introduced and a one-stage operative technic for both mitral and triscuspid valvuloplasty described.

TRICUSPID stenosis rarely exists as a solitary valvular disease. In various autopsy studies it has occurred in 10 to 15 per cent of patients with chronic rheumatic valvular disease.[1, 2] It is most frequently associated with combined aortic and mitral valvular lesions.[1, 2] Mitral stenosis without aortic valve disease is complicated by tricuspid stenosis in about 6 per cent of the instances.[3] The principal symptoms and signs of tricuspid stenosis may be obscured by those of concomitant mitral stenosis, and the diagnosis of the combined lesion is easily missed.

Since scattered case reports have shown that patients with combined mitral and tricuspid stenosis may not improve following mitral valve surgery alone,[3, 5, 6] and since tricuspid stenosis can be surgically corrected, the detection of significant tricuspid stenosis is of paramount importance. This lesion may be strongly suspected from the presence of certain symptoms, signs and changes in the electrocardiograms and roentgenograms. A correct diagnosis may be established by cardiac catheterization and confirmed by exploration of the tricuspid valve.

In the past five years, hemodynamic studies of tricuspid stenosis have been reported in only 10 cases[3-9] and this condition has not been generally recognized.

During the past three years, we have studied, preoperatively, about 100 patients with mitral stenosis by means of cardiac catheterization. Five of these had significant tricuspid stenosis. The clinical diagnosis was made before catheterization in 4 cases and confirmed by operation. The diagnosis in one case was made only in retrospect, during a review of catheterization data, and was subsequently confirmed by autopsy.

The purpose of this paper is (1) to report the results of the clinical and hemodynamic studies of these 5 cases, (2) to emphasize the diagnostic criteria of this condition, (3) to stress the importance and feasibility of tricuspid valvuloplasty in patients with combined mitral and tricuspid stenosis and (4) to introduce a one stage operative technic for both mitral and tricuspid valvuloplasty.

CASE REPORTS

Case 1. M. N. This 31 year old housewife had chorea at age 10. She first developed exertional dyspnea, fatigue, ankle edema and high blood pressure at age 27, during pregnancy. Following

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A preliminary abstract of this paper appeared in Circulation **12:** 792, 1955.

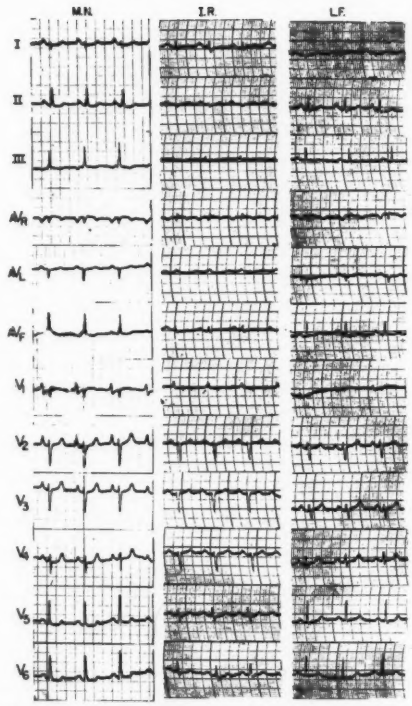

FIG. 1. Electrocardiograms of 3 patients with tricuspid stenosis and sinus rhythm. Note the relatively tall P wave and small QRS complex in lead V_1.

delivery, the edema subsided and the patient felt quite well for about a year. At age 28, she had acute rheumatic fever and was bedridden for about two months. Subsequently, she had progressive exertional dyspnea, lassitude, and intermittent ankle edema. After an episode of acute pulmonary edema the following year, she was digitalized and required intermittent mercurials to keep her edema-free. Several months later, she had another episode of pulmonary edema followed by "pneumonia" and severe hemoptysis, which required three weeks of hospitalization.

On Dec. 2, 1952 physical examination revealed a pallid, noncyanotic woman, who was not orthopneic or dyspneic at rest. The cervical veins were slightly distended without intrinsic venous pulsation. The lungs were clear. The apical heart rate was 108 per minute and the rhythm was regular. The first mitral sound and second pulmonic sounds were accentuated. In the mitral area were heard a grade 2 systolic murmur and a rumbling presystolic murmur. Blowing systolic and early diastolic murmurs were heard along the left sternal border but were also readily heard at the right sternal border. Along either border of the sternum an additional murmur was heard in middiastole. The blood pressure was 140/95 and the liver was just palpable.

A 12 lead electrocardiogram (fig. 1) showed right axis deviation and high peaked P waves indicating right atrial hypertrophy, but no evidence of either right or left ventricular hypertrophy.

Fluoroscopy and roentgenograms revealed generalized cardiomegaly with clear lung fields. The left ventricle overlapped the vertebral column by 2 cm. in the left anterior oblique view. The right ventricle was considerably enlarged, there was also some enlargement of both atria, the right more so than the left.

On Dec. 16, 1952, cardiac catheterization was performed. Blood-gas analysis failed to disclose left-to-right shunting but indicated mild arterial oxygen unsaturation at rest. Following exercise, the arterial blood became normally saturated. The cardiac output and A-V oxygen difference were within normal limits. There was a definite diastolic pressure gradient across the tricuspid valve which was not appreciated at this time (fig. 2). During a review of the intracardiac tracings, a diagnosis of both mitral and tricuspid stenosis was suspected.

Mitral valve surgery was advised but the patient refused. She became steadily worse and was admitted to another hospital where she died on Jan. 22,

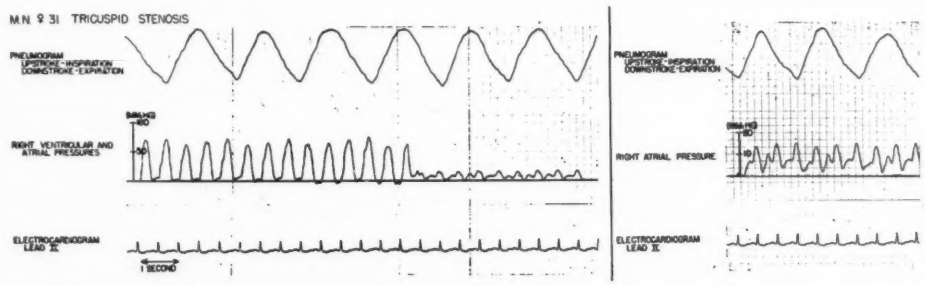

FIG. 2. Intracardiac pressure tracings obtained in a patient (case 1) with tricuspid stenosis and sinus rhythm. The tracing on the left, recorded while the catheter was withdrawn from the right ventricle into the right atrium, shows a diastolic pressure gradient across the tricuspid valve. Giant "a" waves were demonstrated in the right atrial pressure tracing on the right.

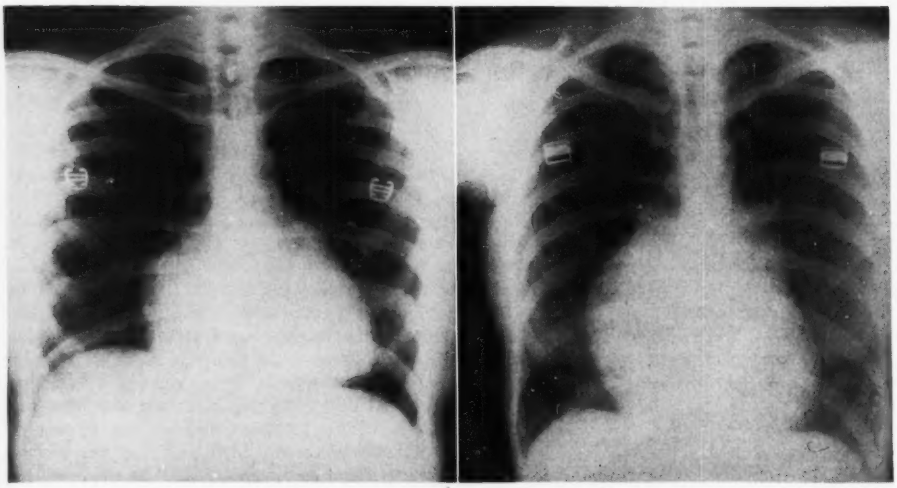

FIG. 3. Roentgenograms of the chest of 2 patients with tricuspid stenosis, case 2 on the left and case 5 on the right.

1953. The pertinent findings on postmortem examination were as follows: There was a bilateral hydrothorax. The heart weighed 400 Gms. and was hourglass in shape, due to enlargement of both atria and ventricles and constriction around the atrioventricular ring. The aortic valve was mildly stenotic. The mitral valve was heavily calcified and fixed, and would not admit the fingertip. The tricuspid valve was deformed and narrowed, and the chordae tendineae were shortened and thickened. There were no endocardial vegetations. Both ventricles were only moderately hypertrophied. The left atrium, pulmonary veins, pulmonary arteries and right ventricle were moderately dilated. The right atrium and venae cavae were greatly dilated. The myocardium and coronary arteries appeared normal. The lungs and liver were passively congested.

Case 2. M. P. A 32 year old housewife, had scarlet fever at age five and pleurisy at age 18, when a heart murmur was heard. At age 20, a diagnosis of mitral stenosis was made. When she was 25 years old, she had an episode of hypotension and a diagnosis of pulmonary embolism was entertained. Her activities were unrestricted until Oct. 1953, when she began to notice exertional dyspnea, swelling of her ankles and pulsation of the neck vessels. In Nov. 1953, she was hospitalized and treated with digoxin and a low salt diet. Her exertional dyspnea became less marked and ankle edema completely subsided. She was then maintained on digitalis therapy.

On Jan. 4, 1954 she was well-nourished, although she looked chronically ill. There was no cyanosis, clubbing of the digits or edema of the legs. The jugular veins were moderately distended. The heart was enlarged to both sides, the rate was 70 per minute, and the rhythm was slightly irregular. The first mitral sound was somewhat accentuated. A grade 3 rumbling diastolic murmur was heard in the mitral area as well as in the lower sternal region. In the tricuspid area the diastolic murmur was intensified by deep inspiration. A grade 2 systolic murmur was heard in the pulmonic area. The second pulmonic sound was louder than the second aortic sound. The blood pressure was 102/70.

A 12 lead electrocardiogram showed atrial flutter with varying A-V block. In lead V_1 the S wave was decreased in amplitude and the R/S approached 1.

Fluoroscopy and roentgenograms of the chest (fig. 3) disclosed a bilaterally enlarged cardiac silhouette. The pulmonary artery and its branches were enlarged. There was definite enlargement of the right ventricle and only slight enlargement of the right atrium. The left atrium appeared normal.

Cardiac catheterization was performed on January 6, 1954. The pertinent data are presented in table 1. On March 2, 1954, mitral and tricuspid valvuloplasty was performed in one stage by a new method.[11]

During the 19 months that have elapsed since surgery, the patient has been free of cardiac symptoms upon ordinary exertion. She takes no medication other than oral prophylactic penicillin. The diastolic murmurs in the mitral and tricuspid areas have diminished in intensity. The heart size is unchanged except for some increase in the size of the left atrial shadow. The electrocardiogram now reveals established atrial fibrillation. Data from postoperative catheterization are given in table 1 and figures 4 and 5.

TABLE 1.—*Blood Flow, Pressures, Resistances in Five Patients with Tricuspid Stenosis*

Case No.		Blood Flow		Blood Pressure (mm. Hg)							Resistance (dynes/sec/cm.$^{-5}$)	
		Cardiac Index (L./M.^{2}/min.)	Stroke Index (ml./M.^{2}/min.)	Pulmonary "Capillary" (m)	Pulmonary Artery		Right Ventricle S/D_1/D_2	Right Atrium			Total Pulmonary	Pulmonary Vascular
					(S/D)	M		M	D_1	D_2		
1. M. N., 31, F	R	2.69	28	32	68/37	49	60/0/4	8	7	9	950	330
BSA = 1.56	E	3.26	25	—	100/58	72	—	—	—	—	—	—
2. M. P., 32, F												
BSA =												
Pre-op., 1.64	R	2.10	35	12	27/15	18	29/1/11	18	15	16	420	140
	E	—	—	—	30/15	21	34/2/5	23	20	24	—	—
Post-op., 1.64	R	2.75	42	22	39/19	29	40/2/13	13	8	14	510	190
	E	—	—	—	51/24	36	50/2/14	15	10	15	—	—
3. L. F., 42, F												
BSA =												
Preop., 1.53	R	—	—	15	33/19	26	39/6/8	13	12	14	—	—
	E	—	—	—	42/25	33	—	—	—	—	—	—
Postop., 1.53	R	2.15	31	13	30/12	19	30/0/7	5	4	8	490	170
	E	—	—	—	38/16	23	32/−2/4	6	5	5	—	—
4. C. B., 46, F	R	3.40	39	26	46/17	27	45/−2/10	16	14	17	520	120
BSA = 1.58	E	—	—	—	51/21	32	—	26	18	20	—	—
5. I. R., 34, F	R	2.42	29	13	24/18	20	31/2/4	9	6	7	320	110
BSA = 1.54	E	2.97	28	—	28/17	21	41/4/6	19	17	18	350	—

R = at rest.
E = after exercise.
M = mean.
S = systolic.
D or D_2 = end-diastolic.
D_1 = early diastolic.
BSA = body surface area in M.^{2}

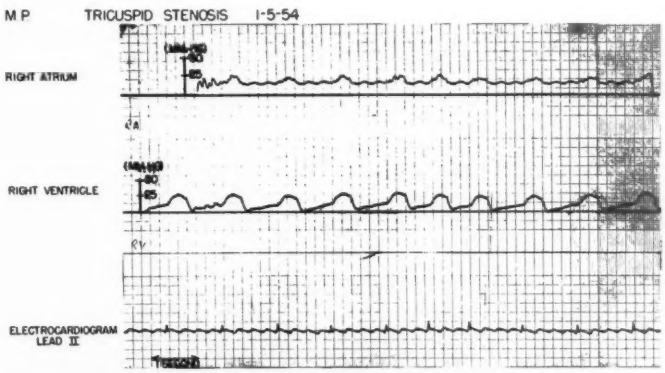

FIG. 4. Simultaneous right atrial and right ventricular pressure tracings obtained through a double-lumen catheter in a patient (case 2) with tricuspid stenosis and atrial flutter. Note the absence of giant "a" wave in the right atrial pressure and the elevated right ventricular end-diastolic pressure.

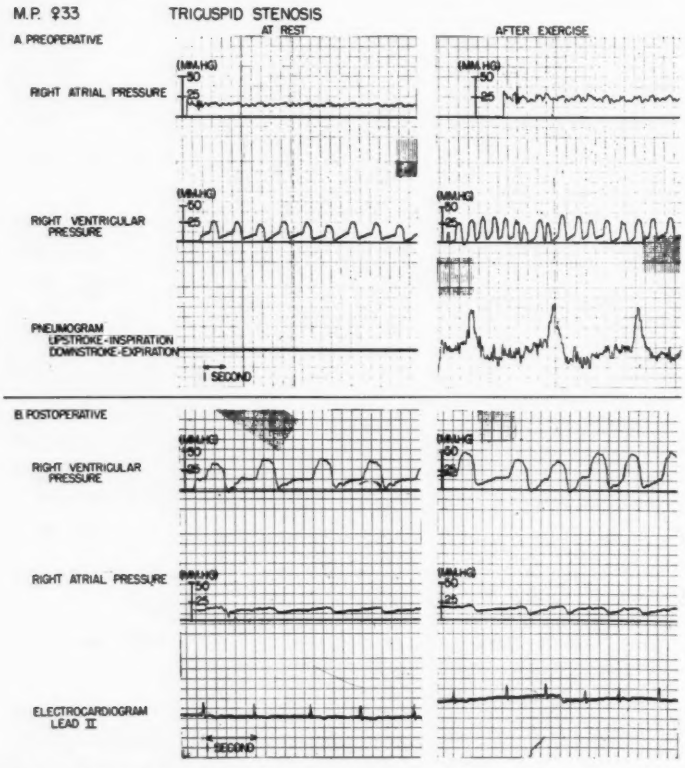

FIG. 5. Right atrial and right ventricular pressure tracings obtained through a double-lumen catheter in a patient (case 2) with tricuspid stenosis before and three months after mitral and tricuspid valvuloplasty. In the preoperative tracings, the right ventricular end-diastolic pressure fell toward normal after exercise. In the postoperative tracings there was no longer any diastolic pressure gradient across the tricuspid valve at rest or after exercise.

Case 3. L. F. A 42 year old housewife had acute rheumatic fever at age 14 and was found to have a heart murmur at age 22. Five years prior to admission, she developed increasing exertional dyspnea and fatigue to the point of inability to walk more than a block. She also noticed pulsation of the neck vessels and frequent palpitation of the heart.

Physical examination showed dyspnea on slight exertion and stasis cyanosis of the face and ear lobes. The jugular veins were distended and a distinct "a" wave was demonstrable. There were classical signs of mitral stenosis. In addition, a rumbling diastolic murmur, exaggerated by deep inspiration, was audible at the tricuspid area. There was a distinct opening snap at the apex and along the left sternal border. The liver was palpable 2 cm. below the costal margin.

An electrocardiogram showed a tall P wave in leads 2, 3 and V_1 and was suggestive of right ventricular hypertrophy (fig. 1). Radiologic examination showed moderate cardiac enlargement with prominent pulmonary vessels, enlarged right ventricle, slightly enlarged left atrium and moderately enlarged right atrium.

Cardiac catheterization showed a diastolic pressure gradient across the tricuspid valve and slightly elevated pulmonary artery and pulmonary "capillary" pressures (table 1). A diagnosis of mitral and tricuspid stenosis was made. Operation was planned in two stages. Mitral valvuloplasty was performed on May 13, 1954. The mitral valve orifice was very small and was estimated to be less than 1 sq. cm. in size. Adequate fracture of the commissures was carried out to about the size of 2 fingerbreadths.

After the operation the patient was not improved, although physical examination showed considerable decrease in the intensity of both the first mitral sound and the rumbling diastolic murmur at the apex. However, the opening snap and the rumbling diastolic murmur along the left sternal border persisted. On July 7, 1954, she developed atrial flutter

with 2:1 A-V block and a ventricular rate of 120 per minute. Digoxin therapy was started and the atrial flutter changed to atrial fibrillation.

Tricuspid valvuloplasty was performed on July 9, 1954. The tricuspid valve orifice was found to be small and the operator could not insert his index finger beyond the first interphalangeal crease. With adequate fracture, the tricuspid valve was considerably enlarged.

Following the second operation, the patient improved steadily and the atrial fibrillation reverted to sinus rhythm. In three months all the physical signs of tricuspid stenosis disappeared and the physical signs of mitral stenosis were minimal. Postoperative cardiac catheterization was performed (table 1). In Oct. 1955, the patient had no cardiac symptoms upon mowing the lawn, climbing stairs or walking on level ground.

Case 4. C. B. This 46 year old married housewife complained of severe fatigue of several years' duration, and swelling of the abdomen of three months' duration. When she was nine years old, she had a febrile illness associated with swollen joints. She was well until the age of 37, when she had sudden onset of acute dyspnea and orthopnea necessitating hospitalization and digitalization. At age 41 intermittent ankle edema appeared. She also noted pulsation of the neck vessels and frequent palpitation of heart. For a year before we examined her, symptoms of fatigue and exertional dyspnea became progressively more severe, resulting in almost complete disability with confinement to bed most of the time. Treatment consisted of digoxin, Diamox and salt restriction.

On physical examination, the patient appeared malnourished and chronically ill. The pertinent findings included erythema of the palms, some stasis cyanosis of the face and distended cervical veins with slight pulsation. The left border of the cardiac dullness was in the anterior axillary line. There was a slight right ventricular precordial heave. The heart sounds were of good quality. At the apex, the first mitral sound was moderately accentuated and was followed by a grade 2 blowing systolic murmur. The second apical sound was followed by a rumbling middiastolic murmur of grade 2–3 intensity, which increased during expiration. Over the tricuspid area were a grade 2 systolic murmur and a grade 2 rumbling diastolic murmur, which became louder during full inspiration. Along the left sternal border, from the second to the fourth intercostal spaces, was a grade 1–2, blowing, decrescendo, early diastolic murmur. The second pulmonic sound was slightly accentuated and split. The lungs were clear, the liver was felt about 4 fingerbreadths below the costal margin, and no peripheral edema was demonstrable.

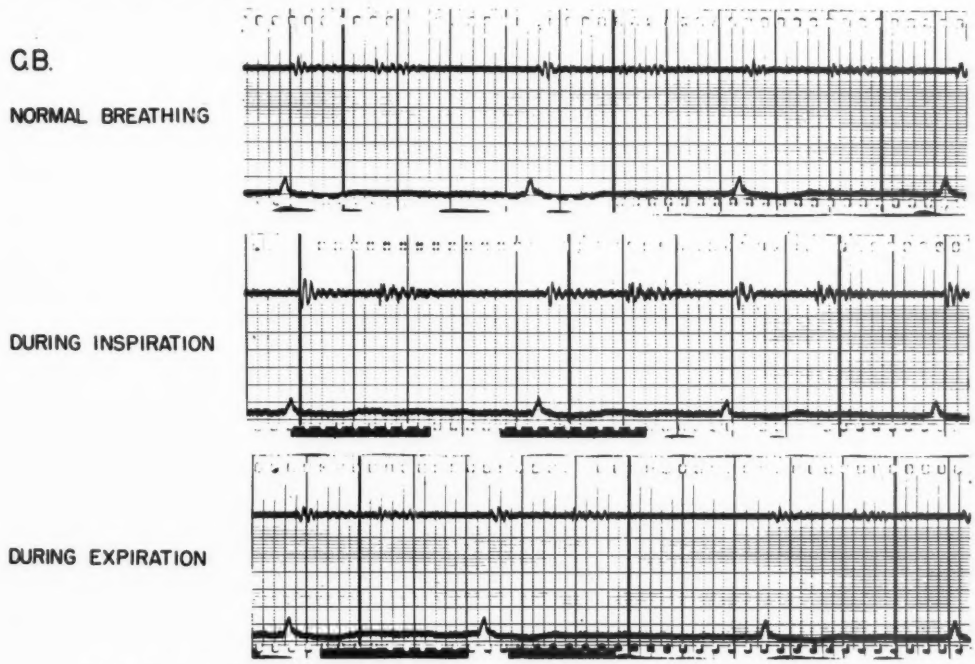

FIG. 6. Phonocardiogram of a patient (case 4) with tricuspid stenosis. The microphone was placed over the tricuspid area. Note the accentuation of the diastolic murmur during inspiration.

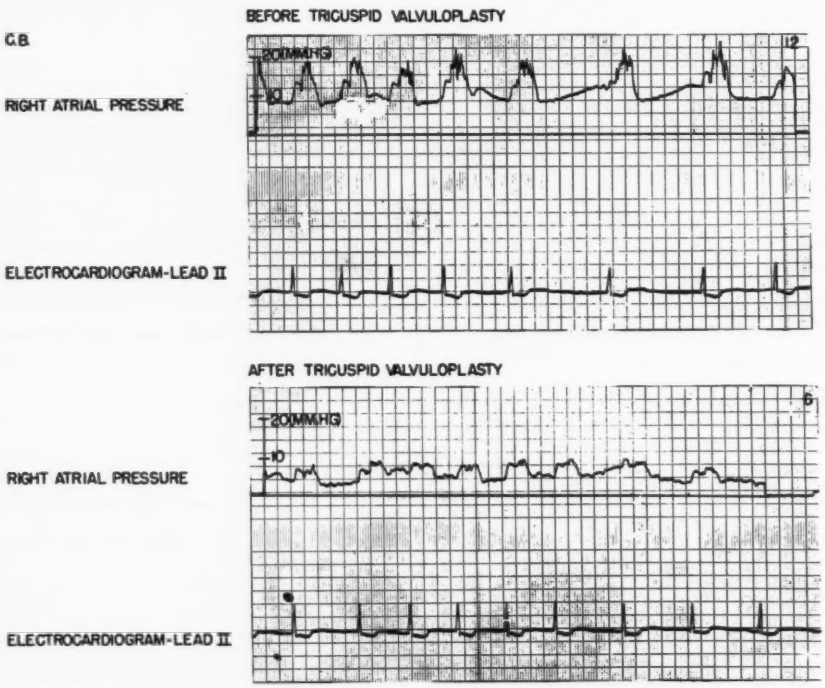

FIG. 7. Direct pressure tracings obtained from right atrium before and immediately following tricuspid valvuloplasty in a patient (case 4) with tricuspid stenosis and atrial fibrillation. The preoperative mean right atrial pressure of 12 mm. Hg was reduced to 6 mm. Hg following operation.

A phonocardiogram confirmed the tricuspid diastolic murmur, which was intensified during inspiration (fig. 6). A 12 lead electrocardiogram showed atrial fibrillation, right axis deviation, and abnormal T waves and ST segments in the precordial leads. There was no hypertrophy of either ventricle. Fluoroscopy and roentgenograms of the chest revealed enlargement of both atria, particularly the right, and of the right ventricle, and questionably the left ventricle. The pertinent data of the cardiac catheterization are tabulated in table 1. Cineangiocardiogram showed retention of radiopaque substance in a large right atrium.

On March 1, 1955, a thoracotomy was performed and revealed a fairly adherent pericarditis. The mitral valve was fibrotic, opened quite widely and admitted 2 fingers; there was a definite regurgitant jet. When the right atrium was entered, the tricuspid valve leaflets were found to be thin and the orifice was estimated at 1.5 sq. cm. The fused posterior superior commissure of the valve was fractured, whereupon the valve opened widely. A slight regurgitant jet felt before the fracture was not altered by the procedure. Before the fracture of the tricuspid valve the right atrial mean pressure was 12 mm. Hg; immediately following the fracture it decreased to 6 mm. Hg (fig. 7). The patient's postoperative course was rather stormy and associated with bilateral hydrothorax necessitating right thoracentesis. There was some increase in her pulmonary congestion or infection. Following digitalis therapy, diuretics and salt restriction, she gradually improved and was discharged after 29 days of hospitalization.

Six months after surgery, she stated that she was less dyspneic on exertion and able to do more housework than previously.

Case 5. I. R. This 34 year old housewife had scarlet fever at age 4. At age 21 a pre-employment examination disclosed cardiomegaly as well as a heart murmur. Her activities were restricted because of one flight dyspnea, fatigue, and mild orthopnea. She had always been subject to frequent respiratory infections, usually associated with wheezing and nonproductive cough. She also noticed moderate pulsation of the neck veins. In October, 1954, digitalis was prescribed, following a respiratory infection associated with severe cough and tachycardia.

In February, 1955, physical examination revealed normal development and nutrition without cyanosis or orthopnea. The cervical veins were slightly distended and there was a distinct "a"

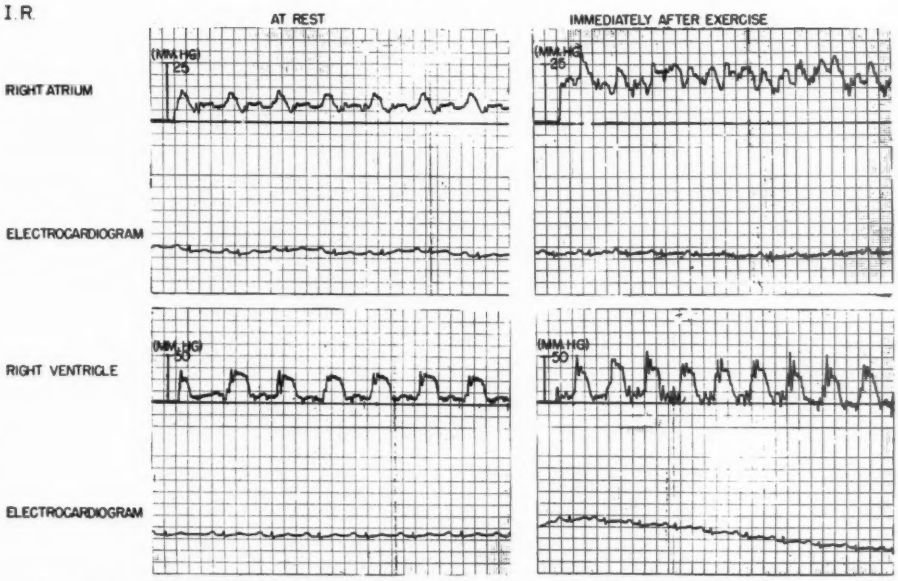

FIG. 8. The right atrial and right ventricular pressure tracings in a patient (case 5) with tricuspid stenosis and sinus rhythm. Note the diastolic pressure gradient across the tricuspid valve at rest, which was greatly exaggerated immediately after exercise. The giant "a" wave in the right atrial tracing is characteristic. The right ventricular diastolic pressure actually decreased after exercise.

wave. Examination of the heart showed the point of maximum impulse to be in the sixth intercostal space along the left midclavicular line. The first mitral sound was slightly accentuated and the second pulmonic sound was louder than the second aortic sound and was split. A blowing decrescendo, early diastolic murmur of grade 2 intensity, accentuated by inspiration, was heard over the base of the heart but maximal along the left sternal border. In addition, a soft systolic murmur was heard over the base. At the tricuspid area there was a grade 3 rumbling middiastolic murmur, which was intensified by inspiration and decreased during expiration. At the apex, there was a middiastolic rumbling murmur of grade 3 intensity with presystolic accentuation. The lungs were clear to percussion and auscultation. The liver was palpable about 2 fingerbreadths below the costal margin. There was no peripheral edema.

A 12 lead electrocardiogram (fig. 1) showed a rate of 90 and a first degree A-V block. The P waves were very broad, tall and notched in leads 1, 2 and aVF. The electrocardiographic position of the heart was vertical. A high peaked P wave was also present in lead V_1. There was no evidence of either right or left ventricular hypertrophy.

Fluoroscopy and roentgenograms of the chest (fig. 3) showed an increased cardiac silhouette with the right heart border projected well to the right of the spine and round in contour. The pulmonary artery segment was normal and the left ventricular border was rounded and prominent. In the right anterior oblique position, both atria appeared enlarged and the pulmonary artery segment was prominent. In the left anterior oblique view, the right ventricular enlargement was quite distinct. On March 22, 1955, cardiac catheterization revealed a diastolic pressure gradient across the tricuspid valve, which was accentuated following exercise (table 1 and fig. 8).

In June, 1955, thoracotomy disclosed moderately severe mitral stenosis for which an adequate valvuloplasty was performed. The tricuspid valve, which would admit no more than the index finger up to the second joint, was considerably enlarged by finger fracture. Mitral valvuloplasty resulted in a fall in left atrial, but no change in right atrial, pressure. Following tricuspid valvuloplasty the right atrial pressure fell. The pulmonary artery pressure changed little throughout. Three months later, the patient claimed marked improvement in exercise tolerance. She was able to do all the housework without symptoms. The cervical veins were no longer distended although a distinct "a" wave was still visible. The size of the heart became smaller and the rumbling diastolic murmur over the tricuspid area was less distinct.

TABLE 2.—*Pertinent Symptoms and Important Findings in Five Patients with Tricuspid Stenosis*

Pertinent Symptoms	No. of Cases
History of acute rheumatic fever	3
History of scarlet fever	2
Severe exertional dyspnea	5
Increased fatigue	5
Marked functional disability	5
Awareness of pulsations in the neck veins	4
Swelling of the legs or abdomen	3
Palpitation of the heart	3
Important Physical Findings	
Distended cervical veins	5
Rumbling diastolic murmur in the tricuspid area, (accentuated by inspiration in 4)	5
Hepatic enlargement	4
Pulmonic second sound slightly accentuated and split	4
Stasis cyanosis of the face	3

COMMENTS

A. Clinical Studies

All these 5 patients were women. Their pertinent symptoms and signs are listed in table 2. Three patients had had acute rheumatic fever and the other 2 had had scarlet fever. All were severely disabled by exertional dyspnea and fatigue, 4 were aware of pulsation in the neck; palpitation and peripheral edema or ascites were present in 3 cases. In agreement with the findings described by McCord and his associates[9] and by Chesterman and Whitaker,[6] the most characteristic physical signs were distended cervical veins and a rumbling diastolic murmur over the tricuspid area. The tricuspid diastolic murmur was intensified during inspiration in 4 patients, in whom the diastolic murmur of mitral stenosis was usually diminished with deep inspiration. The second pulmonic sound was slightly accentuated and split in 4 cases. Even though the patients were greatly disabled, the physical signs of marked pulmonary hypertension were conspicuously absent.[10] Hepatic enlargement was present in 4 patients and 3 had stasis cyanosis of the face.

Electrocardiograms showed sinus rhythm in 3, atrial flutter in 1 and atrial fibrillation in the fifth patient. The P wave was very prominent in all 3 patients with sinus rhythm, particularly in lead V_1. The electrocardiographic position of the heart was vertical in all. Suggestive evidence of right ventricular hypertrophy was noted in only 2 patients.

Roentgenograms and fluoroscopy of the chest showed moderate to marked enlargement of the cardiac size in all patients. The enlargement involved right atrium, pulmonary artery, right ventricle and left atrium. In a patient reported by Trace and co-workers,[5] there was no enlargement of the left atrium. A cineangiocardiogram performed in one patient demonstrated prolonged retention of radiopaque substance in a large right atrium.

B. Hemodynamic Studies

The hemodynamics in patients with predominant tricuspid stenosis have been admirably described by Ferrer and co-workers.[7] The presence of a significant diastolic pressure gradient across the tricuspid valve is emphasized by most workers[4, 6-10]; this is accentuated by exercise and is present regardless of the cardiac rhythm. As pointed out by McCord and his associates,[9] the gradient was more marked during the early diastolic period than during the end-diastolic period.

Small diastolic pressure gradients across the tricuspid valve do not necessarily indicate anatomic stenosis. In another patient, not described in this report, the clinical diagnosis of tricuspid insufficiency was substantiated by finding a "ventricular" contour in the right atrial pressure pattern during exercise. There were physical signs of associated tricuspid stenosis and a consistent diastolic pressure gradient of 2 mm. Hg across the tricuspid valve at rest. At operation it was thought that the valve was purely insufficient.

The elevation of diastolic pressures in the right ventricle in 3 of our patients, (M. P., L. F., C. B.), before operation is difficult to explain. It is not likely that it was due to right ventricular failure, as a consequence of the associated mitral valve disease, since the right ventricular systolic pressures were only mildly elevated. Furthermore, when one of these 3 patients, (I. R.) was exercised, the right ventricular diastolic pressure fell to normal (fig. 8).

In patients with sinus rhythm a giant "a"

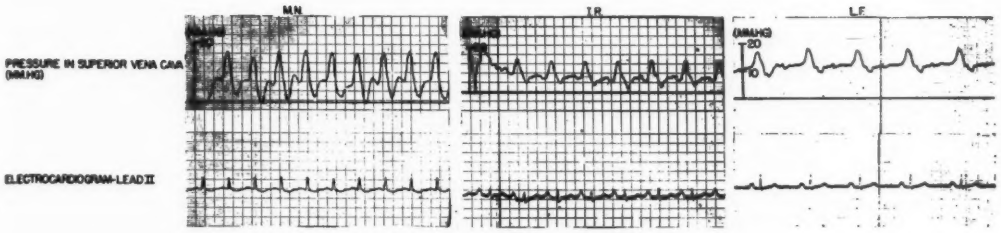

FIG. 9. Blood pressure tracings obtained from superior vena cava in 3 patients with tricuspid stenosis and sinus rhythm. Note the presence of giant "a" wave in each tracing.

wave, produced by vigorous contractions of the right atrium, was seen in the pressure tracings obtained from the right atrium and superior vena cava (fig. 9). The peaks of atrial systole were very high, around 18 mm. Hg in our 3 cases. At the conclusion of atrial systole, the atrial pressure fell rapidly to the lowest point in the cycle, as other workers have noted. We consider this probably an exaggeration of the "x" descent following vigorous systole in a distended right atrium. It did not occur in our 2 patients with atrial fibrillation or flutter. With the opening of the tricuspid valve the right atrial and vena caval pressures did not fall markedly. Ferrer and her associates[7] suggest that, during early diastole, the volume change in the right atrium is small and large right ventricular filling is not accomplished.

The pulmonary artery and pulmonary "capillary" pressures were normal or slightly elevated in 4 patients at rest and rose slightly with exercise. These were distinctly lower than in patients comparably disabled by predominant mitral stenosis. In patient M. N., both the pulmonary artery and pulmonary "capillary" pressures were much higher than in the other 4 patients. At autopsy, the degree of mitral stenosis was considerably more marked than that of tricuspid stenosis. In our experience as well as in that of McCord and associates,[9] the degree of pulmonary hypertension usually varies inversely with the severity of tricuspid stenosis in a patient with combined mitral and tricuspid stenosis.

The resting cardiac index and stroke index were subnormal in all but one patient. With exercise, cardiac index increased slightly but the stroke index actually decreased, although the total pulmonary resistance was either normal or only slightly increased.

C. Surgical Aspects

Combined mitral and tricuspid valvuloplasty was performed in 3 patients with excellent results. Patient 4, whose mitral valve was predominantly insufficient, showed moderate improvement following tricuspid valvuloplasty alone. The operation was performed in one stage in 3 patients and in two stages in 1 patient.

The advent of surgical intervention in any condition requires reappraisal of that pathologic state. It is not uncommon to find the accepted morphology at variance with new kinetic pathologic concepts. Since the advent of satisfactory surgical correction, the limited opportunity for observing tricuspid stenosis permits only preliminary impressions. It would appear that often the fusion bridge is in the anterior commissure. The longest axis of leaflet contact is here, between the anteromedial and anterolateral cusps. Two general patterns of tricuspid stenosis are commonly palpated at the operating table. The first is a residual posterior transverse slit-like orifice where the medial and lateral cusps fuse. The slit-like orifice is made up of the commissure between the lateral and posterior cusps. Tricuspid stenosis is virtually always associated with mitral valve disease, which produces hypertrophy and dilatation of the right ventricle. With such hypertrophy and dilatation of the right ventricle this transverse fissure is stretched taut to produce much more significant stenosis hemodynamically than one might anticipate in the flaccid heart at post-

mortem. The conventional postmortem opening of the heart, in the direction of blood flow, divides the annulus and leaflets of the tricuspid valve in such a way that this type of stenosis is difficult to recognize. This type of lesion may be called "functional tricuspid stenosis." Correction of mitral stenosis alone might so reduce pulmonary hypertension and right ventricular size that the tricuspid annulus could contract and the "functional tricuspid stenosis" might well disappear.

A second form of tricuspid stenosis is more significant and straightforward. It consists of a diaphragm with more or less circular central defect. The stenotic orifice may be as small as 2 sq. cm. This stenotic diaphragm is held as a rigid tambour by its circumferential attachment to the dilated annulus. Enlargement of the annulus is secondary to right ventricular hypertrophy and dilatation, which in turn is secondary to the mitral valve disease. This type of tricuspid stenosis will produce significant clinical and hemodynamic changes and the lesion should be adequately corrected.

A simple technic has been developed for fracturing both mitral and tricuspid valves in one stage through a left thoracic incision.[11] The technic may be summarized briefly as follows: The mitral valvuloplasty is completed after opening the pericardium in the usual way posterior to the phrenic nerve, then the pericardium is loosely approximated and incised again obliquely upward over the pulmonary artery from the phrenic nerve in the direction of patient's right shoulder. The incision is carried over the anterior aspect of the pulmonary conus. Marsupializing sutures are used for traction to rotate and elevate the pericardium gently, from right to left, until the enlarged right atrial appendage appears. With the appendage in the operative field, the usual circumferential purse-string sutures are placed in it and the finger fracture valvuloplasty of the tricuspid stenosis is carried out. The criteria for adequate tricuspid valvuloplasty have not been established, but an orifice of 4 or more sq. cm. would seem to be adequate.

At operation, a decline in the left atrial pressure followed mitral valvuloplasty and a fall in the right atrial pressure followed tricuspid valvuloplasty.

Postoperative cardiac catheterization in 2 patients revealed disappearance of the diastolic pressure gradient across the tricuspid valve, both at rest and after exercise. The pulmonary artery and pulmonary "capillary" pressures rose slightly in one patient and cardiac output increased. The pressures in the pulmonary circuit fell slightly in the other.

Summary

1. Tricuspid stenosis occasionally accompanies mitral stenosis.

2. Distinct findings on physical examination, electrocardiogram and x-ray examination suggest the diagnosis, (1) a diastolic rumbling murmur in the tricuspid area, accentuated by inspiration; (2) prominent "a" wave in the jugular pulse; (3) "P pulmonale" waves in the electrocardiogram; (4) absence of signs of marked pulmonary hypertension or of right ventricular hypertrophy, although the patient is markedly disabled and (5) disproportionate right atrial enlargement by fluoroscopy.

3. The diagnosis is confirmed by a significant diastolic pressure gradient across the tricuspid valve at rest and during exercise.

4. In a patient with combined mitral and tricuspid stenosis, the expected improvement may not occur unless both mitral and tricuspid valves are fractured.

5. The concept of true tricuspid stenosis and "functional tricuspid stenosis" was introduced and a 1-stage operative technic for both mitral and tricuspid valvuloplasty is described.

6. With an increased awareness of its existence, more cases will be correctly diagnosed and benefited by proper surgical treatment.

Addendum

Since the presentation of this paper an excellent paper entitled "The Diagnosis of Tricuspid Stenosis" by Drs. Ronald Gibson and Paul Wood was published in the British Heart Journal **17:** 552 (Oct.), 1955. The clinical and hemodynamic features of their 14 cases were very similar to those reported in this paper.

Acknowledgment

We are grateful to Dr. R. Taylor, Auburn, New York, and Dr. J. W. Walker, Geneva, New York, for permission to include the description of the terminal illness and autopsy findings of Case 1(M. N.). We are indebted to Dr. Andrew Dale for permission

to include the third case (L. F.). He performed both mitral and tricuspid valvuloplasty on this patient.

Summario in Interlingua

1. Stenosis tricuspide accompania a vices stenosis mitral.

2. Le diagnose se suggere per le sequente distincte constatationes physic, electrocardiographic, e roentgenographic: (1) Un rolante murmure diastolic in le area tricuspide, accentuate per inspiration. (2) Un prominente unda "a" in le pulso jugular. (3) Undas "P pulmonal" in le electrocardiogramma. (4) Absentia de signos de marcate hypertension pulmonar o de hypertrophia dextero-ventricular, in despecto del facto que le patiente es marcatemente invalidate. E (5) un disproportionate allargamento dextero-atrial, visibile per fluoroscopia.

3. Le diagnose se confirma per le constatation de un significative gradiente de pression diastolic a transverso le valvula tricuspide in stato de reposo e durante exercitio.

4. In un patiente con combinate stenosis mitral e tricuspide, le expectate melioration non pote occurrer si non le valvulas tanto mitral como etiam tricuspide es fracturate.

5. Le concepto de ver stenosis tricuspide e de "functional stenosis tricuspide" esseva introducite. Es describite un technica a operation unic pro valvuloplastia mitral e etiam tricuspide.

6. Con le diffusion del information que iste condition existe, plus numerose casos de illo va esser diagnosticate correctemente e va profitar del appropriate tractamento chirurgic.

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Thromboembolic Complications Following So-called "Good Risk" Cases of Myocardial Infarction

By ADOLFO DE FRANCISCO, M.D., AND IRVING S. WRIGHT, M.D.

Thromboembolic complications frequently occur following myocardial infarction. Following the general acceptance of anticoagulant therapy for the treatment of myocardial infarction, there have been some authors who have recommended that this therapy be withheld from "mild cases," unless they develop thromboembolic complications. It is the belief of the present authors that this is not justified unless there are contraindications for anticoagulant treatment, provided that proper facilities are available. Summaries of experience with 14 so-called "good risk" cases of myocardial infarction who developed a total of 18 certain and 4 probable thromboembolic complications are presented. As a result, there were 4 major amputations in 3 patients, 1 of whom died. Other complications are discussed in detail.

IT is a well known fact that thromboembolic complications frequently occur in patients who have suffered from myocardial infarction. In the series reported by the Committee on Anticoagulants of the American Heart Association, 26 per cent of the patients who received routine treatment without anticoagulants developed either one or more thromboembolic complications during the 6-week period of observation that followed the initial episode of coronary occlusion with infarction. In 19 additional series reported in the literature,[1] an average of 18.9 per cent of patients who were not treated with anticoagulants developed thromboembolic complications.

Pathologic studies have demonstrated the high incidence of mural thrombi that develop in association with myocardial infarction.[2, 3] The figures published by different investigators have varied, the highest being 66.9 per cent reported by Garvin[4] and 83 per cent in the series of Levine and Brown.[5] Intracardiac thrombosis undoubtedly represents the main source of embolization, the formation of mural thrombi occurring most frequently in the left ventricle. Thrombosis of the veins of the pelvis and lower extremities is often the source of pulmonary emboli.[6]

Although thromboembolic complications usually develop during the first few weeks that follow an episode of myocardial infarction, they may also occur after months or even years of the attack. Levine[7] has pointed out that mural thrombi may remain pocketed in the heart chambers for many years, and represent a continuous threat of embolization. Towbin,[8] in a recent study, was able to demonstrate pathologic evidence of multiple cerebral embolism in 11 patients with chronic organic brain disease who had had old myocardial infarctions, in some cases several years prior to the development of cerebral embolism. All of them harbored intracardiac mural thrombi.

The value of anticoagulant therapy in the management of coronary thrombosis with myocardial infarction has been substantiated by many investigators. The results presented by the Committee on Anticoagulants of the American Heart Association[1] and the data reported by others[9-12] indicate that anticoagulant therapy markedly reduces the incidence of thromboembolic complications as well as the death rate of patients who have suffered from myocardial infarction.

After the Committee recommended that anticoagulant therapy be given to all patients with myocardial infarction provided no contra-

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indications were present, several authors expressed doubts as to the advisability of instituting this form of therapy in every case of myocardial infarction. They have concluded that the selection of patients for anticoagulants should be based on certain prognostic criteria.

Russek and associates[13-15] suggested that patients with myocardial infarction be classified as "good risk" or "poor risk" cases according to the signs and symptoms present on the day of admission to the hospital, and have proposed the criteria for such a classification. They consider the patient to be a "poor risk" case, when one or more of the following poor prognostic factors are present during the first 24 hours of hospitalization: (1) evidence of a previous myocardial infarction; (2) intractable pain; (3) extreme degree or persistence of shock; (4) significant enlargement of the heart; (5) gallop rhythm; (6) congestive heart failure; (7) atrial fibrillation or flutter, ventricular tachycardia, or intraventricular block; (8) diabetic acidosis, marked obesity, previous pulmonary embolism, varicosities in the lower extremities, thrombophlebitis (past or present), or other states predisposing to thrombosis. Contrariwise, a patient not presenting any of the signs mentioned above during the first 24 hours of hospitalization is considered a "good risk" case.

According to Russek's report, the "good risk" cases have a low mortality rate as well as a low incidence of thromboembolic complications as compared with "poor risk" cases. Therefore, he does not consider the use of anticoagulant therapy indicated in those cases, since "the incidence of hemorrhagic complications and death due to anticoagulant drugs, even when prescribed by the most competent investigators, appears to outweigh any benefit which such therapy may confer in milder cases."[16] He concludes that anticoagulant therapy should be reserved for properly selected "poor risk" cases in which the mortality rate and the incidence of thromboembolism are markedly elevated. There have been several other workers who have expressed similar opinions.[17, 18]

The Committee divided the cases of its series into good and poor risk groups, following criteria similar to and even more rigid than those of Russek and co-workers. Only 17 per cent of the cases could have been classified as "good risk" cases as contrasted with 47 per cent reported by Russek. Among the group of "good risk" cases of the Committee who were not receiving anticoagulant therapy, 23 per cent developed thromboembolic complications, including three deaths if an age of 80 or over is not defined as a poor risk criterion, and one death if the old age is considered to aggravate the prognosis. This is in sharp contrast with Russek's report of less than 1 per cent of thromboembolic complications in his group of "good risk" patients.

We believe that the estimation of prognosis of a given case of myocardial infarction, based on the signs and symptoms present during the first 24 or 48 hours cannot be made with any degree of certainty. Halpern and co-workers[19] recently analyzed a group of 107 patients who fulfilled the criteria for the diagnosis of acute myocardial infarction, and estimated the prognosis when the patient was first examined, and again in 24 and 48 hours. They found that in 29 per cent of their patients it was necessary to change the prognosis during the first 48 hours of hospitalization. Manchester[20] has also attempted to classify 350 patients as "good" or "poor risk" cases. He found that it was necessary to change the category of 25 per cent of his "good risk" cases to "poor risk," and he also noted that 33 per cent of his "poor risk" cases had completely uncomplicated recoveries. Many other workers in this country and abroad[21-23] have agreed that it is impossible to determine with certainty the prognosis of an acute myocardial infarction during the first 24 or 48 hours of the attack.

At the International Conference on Blood Coagulation held in Switzerland in 1954, a panel was held on the problems of myocardial infarction. There was complete unanimity among the members that to base treatment on such an attempt to classify patients was not warranted, and that all patients suffering from myocardial infarction should receive anticoagulants, if adequate facilities were available and unless there were other contraindications.[24]

One of the difficulties in the classification of

a patient as "good" or "poor risk," following the criteria indicated by Russek and his group, is represented by the fact that no definitions have been given of what they consider as "significant enlargement of the heart," "intractable pain," and "other conditions predisposing to thrombosis." This vagueness, in some instances, makes it difficult to decide whether or not the patient should be considered as a "good risk" or "poor risk" case during the first 48 hours.

Moreover, even if a case is believed to be a mild form of coronary thrombosis, it becomes extremely hazardous to predict with certainty that the patient will do well and that no thromboembolic complications will arise. This is clearly demonstrated in patients who have sustained the so-called silent type of coronary occlusion, in which peripheral embolization may be the presenting symptom of myocardial infarction as in some of the cases reported by Lary and De Takats.[25] It is also underscored by the rather frequent sudden death that occurs in patients who have had no previous evidence of cardiac disturbances.

The purpose of this paper is to report on thromboembolic complications occurring in the so-called mild or "good risk" cases of myocardial infarction. We have selected 14 patients who sustained mild attacks of myocardial infarction and fulfilled Russek's criteria of "good risk" cases. All of them were untreated or inadequately treated with anticoagulants, prior to their thromboembolic complications.

The case histories were selected from a group of patients with myocardial infarction seen at The New York Hospital and from the private practices of members of the Vascular Section of the Department of Medicine at The New York Hospital, Cornell University Medical School Center.

Case Reports

Case 1 (S.R. 618371). A few hours prior to admission, a 69 year old man was picking up a kerosene can and moving it a few feet, when he suddenly noted the onset of sharp pain in the right hand. Shortly thereafter this pain extended up to the lower part of the forearm. Simultaneously, the hand became cold and functionless.

His past history, on close questioning, disclosed that he had developed slight precordial pressure on walking 2 blocks during the 3 months prior to admission. This "pressure" was of such a mild degree that he did not consider it seriously, nor did he go to his doctor.

At the time of admission, he had a blood pressure of 150/90, a pulse rate of 82 per minute, and a temperature of 99.6 F. The heart and lungs were unremarkable. On physical examination it was evident that the patient had an acute occlusion at the level of the brachial or the axillary artery. A chest film revealed some enlargement of the left ventricle. An electrocardiogram disclosed evidence of a recent infarction of the anterior wall.

The patient was treated with vasodilators and blocks of the brachial plexus. Anticoagulant therapy was not used in this case because shortly after admission the patient had a hematemesis of undetermined origin. Despite the therapy employed, the extremity became gangrenous and a midarm amputation had to be performed on the thirteenth hospital day. In the immediate postoperative state, a transitory episode of mental confusion and right facial weakness occurred, which cleared up shortly thereafter. The patient was followed in clinic for over a year, until January 1953.

This case represents a mild coronary thrombosis that remained undiagnosed owing to the paucity of symptoms presented by the patient before the thromboembolic complication took place. It illustrates the serious outcome that may sometimes occur in so-called mild myocardial infarctions.

Case 2 (M.S. 696317). A 50 year old white woman was admitted to The New York Hospital on Nov. 5, 1954, complaining of numbness in the left leg of 9 hours' duration.

Six weeks prior to admission the patient began to develop occasional episodes of chest pain. The cardiac origin of this was not recognized at the beginning. She was treated with various medications, mostly sedatives, until finally, two and one-half weeks prior to admission, a diagnosis of myocardial infarction was confirmed and the patient was taken to another hospital. She was treated with bed rest and received some anticoagulant therapy over a period of 2 weeks. Two days prior to admission to The New York Hospital, after dicumarol therapy had been interrupted, the undilute prothrombin time was 17 seconds against a control of 15 seconds. This, of course, was not a protective level.

On arrival, she was complaining of cramps in the left leg and stated that the numbness had been present for 9 hours. On physical examination she had a blood pressure of 170/110, a pulse rate of 80 per minute, and a temperature of 99.3 F. The lungs were clear. The heart was not enlarged; the sounds and the rhythm were normal, and there were no murmurs. There were signs of arterial insufficiency in both legs, particularly in the left, where only the femoral pulse was present. The left leg was cool

below the knee. An x-ray film of her chest was reported as being within normal limits. An electrocardiogram revealed evolutionary changes of a myocardial infarction of the anterior wall.

The patient was started again on anticoagulant therapy. However, gangrene developed and, later on, demarcated at the base of the left hallux. The patient was discharged on the sixty-ninth hospital day, to continue with anticoagulants on an ambulatory basis. She was followed in the Vascular Clinic. Early in March 1955, she developed self amputation of the toe. At present, she is being followed at the Vascular Clinic.

This patient had a mild attack of myocardial infarction and was treated with anticoagulants for only two weeks—too short a period of time. Two days after discontinuing dicumarol, when her prothrombin time had returned to normal, she suffered an embolus or thrombosis that produced gangrene of a toe, causing its subsequent amputation.

Case 3 (M.L. 703473). A 56 year old white man had a mild coronary occlusion on Dec. 24, 1954. He was treated at home with bed rest and papaverine. No anticoagulants were administered. A month later, after having had a bowel movement in a bedpan, he noted the sudden onset of pain in the left foot associated with coolness and numbness. Over the next few days he was given vasodilators and gradually started to ambulate, but he complained of pain in the anterior sole of the left foot on walking a few steps.

He was admitted to The New York Hospital on Feb. 15, 1955. On arrival his blood pressure was 120/88, pulse rate 92 per minute, and his temperature was 96.4 F. The heart was not enlarged. A normal sinus rhythm was present and no murmurs were heard. Examination of the lower extremities revealed signs of arterial insufficiency, more marked on the left side. Oscillometric readings were absent on the left leg and markedly reduced on the right. There were electrocardiographic changes of evolution of a myocardial infarction of the anterior wall.

The patient was placed in an oscillating bed and given Marcumar. He started to ambulate early in March and was discharged on March 12, 1955, very much relieved but without changes in the physical findings of his lower extremities.

This patient sustained a myocardial infarction of such mildness that it was not considered necessary to hospitalize him, and he was treated conservatively at home. Despite the mildness of the case, a month later he suffered an embolus to the terminal aorta, with subsequent fragmentation of the clot. Although no gangrene developed, the patient was left with arterial insufficiency of his lower extremities, secondary to the embolic complication.

Case 4 (E.F. 268739). A 46 year old white man was admitted on June 20, 1940, with gangrene of the right leg.

Seventeen days prior to admission, while shaving himself, this patient experienced the sudden onset of cramplike precordial pain, associated with mild dyspnea and aching in both arms. These symptoms subsided completely upon the administration of morphine. An electrocardiogram revealed evidence of a myocardial infarction, and the patient was advised by his private physician to rest in bed at home—but he was given no more specific therapy.

Eight days later he felt that his right leg was "swelling up." Pain developed in the leg and later it became anesthetic and functionless. Two and a half days later gangrene developed in the toes and extended to the entire foot and the lower leg.

Physical examination disclosed a well developed and well nourished white male, appearing chronically ill but not acutely distressed. Blood pressure was 135/84, pulse rate 80 per minute, and temperature 99.3 F. The heart, both clinically and on x-ray examination, was unremarkable. The abdomen was slightly distended. The gangrene was beginning to demarcate 5 cm. below the knee. The white blood cell count was 22,000, with shift to the left An electrocardiogram confirmed the existence of a myocardial infarction of the anterior wall.

The hospital course was stormy. Two days after admission, the patient had a hematemesis of 240 ml. On June 29, 1940, he developed sudden pain in the left leg with clinical evidence of an acute arterial occlusion of the limb and subsequent development of gangrene. On the twenty-second hospital day, a right midthigh amputation was performed, followed by amputation of the left leg at the same level on the fiftieth hospital day.

A month later, on September 14, 1940, he suddenly developed tachycardia, cough and bloody sputum. On examination of the chest, there was slight dullness to percussion, and rhonchi were heard in the right base. Small pleural effusions in the oblique fissures of both sides and some atelectasis of the right middle lobe were seen on x-ray study. The electrocardiographic findings were consistent with pulmonary embolism. Shortly thereafter, the blood urea nitrogen started to rise; the CO_2 began to drop, and the patient died on Sept. 27, 1940, 99 days after admission and 116 days following the onset of his illness.

This case clearly illustrates the fact that so-called mild myocardial infarction may be followed by thromboembolic complications that lead to a disastrous outcome. A man without a previous history of heart disease developed a mild attack of myocardial infarction. A week later he suffered a series of embolizations to his legs and his lungs, with the development of gangrene that required bilateral amputation of his lower extremities, and he finally died almost four months after the coronary occlusion.

Case 5 (F.P. 75041). A 58 year old white man was admitted to Doctors' Hospital on July 16, 1952,

after having noted the sudden onset of numbness and coldness of his right foot.

A week prior to admission, after a transcontinental motor trip, the patient complained of having some general fatigue without any evidence of cardiac symptoms. For this reason he remained in bed for a day, but was able to resume his normal activities later on. There was no previous history of cardiovascular disease.

On physical examination he was found to have a blood pressure of 140/80, a pulse rate of 110 per minute, and a temperature of 100.5 F. His heart was not enlarged, the rhythm was regular and there were no murmurs. Pulses and oscillometric readings were absent on the right thigh above the knee and were diminished in the left ankle. An electrocardiogram revealed that the patient had sustained what appeared to be a recent myocardial infarction of the posterior wall.

Within three hours of admission, a right femoral embolectomy was performed by Dr. Jere Lord. While a large clot was removed, it was clear that terminal vessels of the leg had been occluded by fragments of the embolus. Subsequently anticoagulant therapy was initiated. However, in spite of careful management, the leg became gangrenous, and a low thigh amputation was carried out on the thirteenth hospital day. The patient had an uneventful postoperative course and was discharged on September 17, 1952.

This case represents a typical silent type of myocardial infarction with peripheral embolization and loss of a limb.

Case 6 (F.S. 76815). In October 1934, a 45 year old man was admitted to The New York Hospital. A week before he had developed pain in the right chest, exacerbated by deep inspirations. The pain subsided rather quickly, but soreness in the right shoulder persisted for several days. Forty-eight hours following the onset of his illness, he coughed up small amounts of clotted blood. Shortly thereafter the patient experienced dysuria, and red blood cells were demonstrated in the urine.

The patient was referred to the hospital by his private physician On admission he appeared moderately acutely ill. He had a temperature of 102 F., and the blood pressure was 140/90. Examination of the lungs revealed signs of consolidation in the right base. Heart sounds were of good quality and the rate was 130 per minute. There was a soft, low-pitched systolic murmur inside the apex and a questionable apical gallop. The laboratory studies showed a leukocytosis of 10,000. X-ray films were consistent with the diagnosis of pulmonary infarction; there was haziness of the right middle lobe; the heart shadow was slightly increased, and there was an enlarged aortic area. An electrocardiogram showed small Q waves in lead I, and deep Q waves and inverted T waves in lead IV. The patient recovered and was discharged on the twenty-second hospital day.

In 1943, at the age of 54, he was admitted to the hospital with a cerebrovascular accident that left him with a right hemiplegia. Three years later he went into congestive heart failure with atrial fibrillation and finally died in 1948.

At autopsy the heart weighed 600 Gm. There was evidence of old scarrings. The right atrium contained large mural thrombi. There was an old 3-centimeter indurated area of fibrosis in the right lower lobe, corresponding to the healed pulmonary infarction. Multiple infarcts were found in the kidneys and the spleen.

This patient had a mild myocardial infarction at the age of 45, and a few days later he developed a clinical picture suggestive of pulmonary infarction. The autopsy many years later demonstrated old scarring in the myocardium and an area of fibrosis in the right lung, corresponding to an old pulmonary infarction.

Case 7 (M.M. 407972). A 62 year old man was admitted to The New York Hospital on December 21, 1950, with a diagnosis of optic neuritis, which was treated with ACTH. The patient had had no symptoms related to his cardiovascular system. Five days after admission a routine electrocardiogram revealed evidence of a myocardial infarction of the anterior wall. Physical examination disclosed a blood pressure of 135/78 and a pulse rate of 80 per minute. The heart sounds were normal, and no murmurs were heard. An x-ray film of the chest showed the heart to be of normal size, with elongation and tortuosity of the aorta. Subsequent electrocardiograms showed evolutionary changes of coronary occlusion. No anticoagulants were given.

Twenty days after admission the patient developed chest pain not related to effort, breathing or coughing. Rales were found in both bases, particularly in the left, and an x-ray film of the chest showed slight changes in the left costophrenic angle. A diagnosis of pulmonary infarction was entertained. Six days following this episode he suddenly complained of numbness in the left foot. Physical examination showed coldness of the foot, absent pulses, and negative oscillometric readings below the knee. In addition, he had a transitory loss of consciousness that might well have represented a small embolization to his brain. A spinal puncture revealed normal findings. Following this, the patient received anticoagulant therapy for six weeks and recovered satisfactorily.

This case illustrates the development of multiple thromboembolic complications, (lung, leg and probably brain), in a man who had sustained an asymptomatic myocardial infarction, which would be classified as a "good risk" case.

Case 8 (K.P. 419489). A 56 year old white man was admitted to The New York Hospital on Au-

gust 14, 1945. Two days prior to admission, while fighting a fire, he inhaled smoke and shortly thereafter experienced pain in the chest radiating to the back and the arms, and associated with some nausea, sweating and weakness. The pain subsided after several hours.

On admission, the blood pressure was found to be 120/70 and the pulse rate to be 110 per minute. Examination of the lungs showed a few fine moist rales at the right base. The heart was not enlarged; the rhythm was regular and there were no murmurs. A chest film was within normal limits. An electrocardiogram disclosed evidence of acute myocardial infarction.

The initial hospital course was unremarkable until the tenth day, when he suddenly complained of severe pain and burning sensation in the left leg. Two days later the right leg also became painful and the pain spread up to the groins. There was evidence on physical examination that he had sustained a saddle embolism with fragmentation of the clot and involvement particularly of the left leg. He recovered and left the hospital on Nov. 1, 1945, with arterial insufficiency in both legs, to be followed in the Vascular Clinic.

Eight years later, in 1953, he was readmitted to the hospital and died of primary carcinoma of the liver. At autopsy, the heart weighed 390 Gm. There was an old, 4 by 6 cm., left apical zone of infarction limited by a thin layer of myocardium. There were also dilatation of the left ventricle and a small thrombus in the same chamber.

This represents another case of arterial insufficiency of the lower extremities secondary to peripheral embolization, following what was initially a very mild infarction. It is interesting to observe that the autopsy demonstrated mural thrombi in the left ventricle eight years after the infarction had occurred.

Case 9 (A.P. 385558). A 40 year old man was admitted to The New York Hospital on May 12, 1944. Ten hours prior to admission, following sexual intercourse, he developed severe pain behind the sternum, radiating posteriorly to the back and the shoulders. The pain was associated with sweating and subsided in an hour, although a slight precordial discomfort persisted intermittently until arrival at the hospital.

The past history was unremarkable except that he had rheumatic fever at the age of 10. Physical examination revealed a well nourished, well developed, healthy looking man, complaining of retrosternal distress. Vital signs were temperature, 102.2 F.; pulse rate, 110 per minute; blood pressure, 134/98; lungs were clear. Examination of the heart revealed a normal sinus rhythm. The point of maximum impulse was found 8 cm. outside the midsternal line in the fourth left intercostal space. There was a soft, apical systolic murmur. A friction rub appeared the day after admission, and persisted, on and off, for four days. An electrocardiogram disclosed evidence of coronary occlusion with infarction of the anterior wall. A portable chest film suggested some enlargement of the heart, particularly of the left ventricle.

On the fifth hospital day, when he appeared to be doing well, he developed fever and signs of consolidation of the right base, occurring without chest pain or hemoptysis. The course of the fever was not altered by the use of sulfadiazine. The possibility of a pulmonary infarct or pneumonia was considered. Two weeks later the patient suddenly developed lumbar pain that persisted for several days but gradually subsided. The pain was associated with albuminuria, hematuria and fever. A diagnosis of renal infarction was suggested. He finally recovered and, at the time of discharge on July 6, 1944, the signs of pulmonary consolidation had disappeared and the urine was clear.

This middle-aged man sustained a mild infarction and developed two thromboembolic complications over a period of three weeks after the onset of his illness. The initial chest pain was severe but subsided in an hour. Thereafter, a mild precordial discomfort persisted intermittently for several hours. Severe pain of one hour's duration would not usually be considered as intractable. If it were to be so interpreted, this patient would be considered as a "poor risk" case. This illustrates the difficulty in applying this specific point of the prognostic criteria that have been suggested.

Case 10 (M.P.M. 639901). A 52 year old hospital orderly was admitted to The New York Hospital on July 7, 1954. During the four months prior to admission, the patient had developed several episodes of left anterior chest pain on exertion. The pain was always relieved by rest. Seventy-two hours prior to admission he was seized with a severe aching sensation in the lower sternal area, associated with some nausea and sweating. The symptoms quickly subsided. On the day of admission he again complained of chest pain, this time radiating to the back and spreading down the left arm.

Physical examination revealed a mildly obese, moderately acutely ill, white man. Blood pressure was 130/90, pulse rate 76 per minute, and temperature 102.2 F. The heart was displaced to the left with the point of maximum impulse in the fifth intercostal space, 2 centimeters outside the midclavicular line. The heart sounds were normal, and there were no murmurs. Fine rales at the bases were present according to one observer. Slight tenderness was found in the right calf, and the dorsalis pedis pulse was absent on that side. An x-ray film of his chest was reported as showing a "right midlung density that represents either disk atelectasis or pulmonary infarct." The electrocardiogram showed evidence of a recent myocardial infarction of the posterior wall. Evolutionary changes were demonstrated in subsequent tracings. The patient was

started on dicumarol therapy upon admission, and was discharged on the forty-third hospital day.

He was then referred to the Vascular Clinic, complaining of intermittent claudication on walking two city blocks. Physical examination showed evidence of arterial insufficiency of both legs, (mostly of the right), with absent oscillometric deflections and pulses below the knee.

This patient never had symptoms suggestive of arterial insufficiency of the lower extremities prior to the onset of this illness. Tenderness in the right calf, with an absent dorsalis pedis pulse on that side, was discovered on admission. When he left the hospital, marked intermittent claudication was present, and there were physical findings of impaired arterial circulation of both legs that were not present previously. It seems likely that he had a saddle embolus that disintegrated and descended into the smaller arteries of his legs. Anticoagulant therapy was instituted shortly after admission to prevent the propagation of these clots and to prevent additional thromboembolic complications.

Case 11 (R.M.M. 651703). A woman, aged 69, was admitted to the hospital on March 15, 1953, having had two bouts of hemoptysis during the 24 hours prior to admission. These were associated with moderate tightness in the lower sternal area and difficulty in breathing. On arrival, she expectorated bright, red blood and again complained of retrosternal tightness. Her past history was of interest in that 15 years earlier she had had a small hemoptysis of unknown etiology.

Physical examination revealed her lying quietly in bed without significant discomfort. Temperature on admission was 99.5 F., and a low grade fever persisted for over a week. Respirations were 28 per minute, pulse rate was 84 and blood pressure was 170/110. The lungs showed tactile fremitus and rales at the right base. She had a normal sinus rhythm with occasional premature beats. The heart was moderately enlarged, both clinically and on x-ray examination, and there was a faint apical systolic murmur. The second aortic sound was louder than the second pulmonic sound. A roentgenogram of her chest failed to reveal any pulmonary disease. The heart shadow was slightly increased in size, and there was elongation and calcification of the aorta. Laboratory analysis included a white cell count that showed a leukocytosis of 13,000, with slight deviation to the left.

A bronchoscopy performed on the fifth hospital day was entirely negative. The patient left the hospital on the ninth day. An electrocardiogram made after the patient had been discharged showed evidence of recent coronary occlusion with infarction.

The symptoms and physical findings in this case suggest the possibility that this patient had a pulmonary infarction that could not be clearly differentiated on x-ray films. This occurred in a patient who sustained a recent silent coronary occlusion, demonstrated by evolutionary changes of myocardial infarction in the tracing.

Case 12 (E.C.). This patient was seen in the office of one of us (I.S.W.) on April 12, 1955. Two months prior to his visit he had developed pain in the left shoulder, radiating down the left arm. Oral medication and diathermy did not help him and the pain persisted at the time of his visit to the office. One week after its onset, he developed pain in the left leg on walking, with a resultant intermittent claudication at a distance of about 200 feet. At no time had he had pain in the chest or in the retrosternal area. He had not noticed any relation of the pain to exertion.

Physical examination revealed a blood pressure of 140/88. The lungs were clear. The heart was in normal sinus rhythm, with sounds of fair quality; no murmurs were heard. The liver edge was palpable 2 fingerbreadths below the costal margin. Examination of the extremities showed the left foot to be cooler than the right. There was 1+ rubor on dependency and 1+ pallor on elevation of the left foot. In the right leg the femoral pulse was felt, but the popliteal, dorsalis pedis and posterior tibial pulsations were absent. Oscillometric readings showed marked diminution in the left leg as compared with the right. An electrocardiogram indicated evidence of a myocardial infarction that had occurred in the recent past, from which the patient was apparently recovering.

This patient had a mild myocardial infarction that was silent insofar as retrosternal pain is concerned. The marked diminution of the circulation of his left leg was probably produced by an embolus, although the possibility of a coincidental occlusion from a thrombosis cannot be completely ruled out.

Case 13 (O.M. 527530). A 40 year old woman was admitted to the hospital on Dec. 10, 1948.

Seven days prior to admission, she awoke with a dull, aching pain and a sense of pressure over the lower anterior chest. The symptoms gradually subsided in 2 or 3 hours. She went to work that day and complained of some light-headedness. On the next day the patient awoke with squeezing lower anterior chest pain that was relieved with an injection, but she noted the persistence of a dull, aching sensation the rest of the day. Two days later she developed severe shooting pain in the right flank, spreading anteriorly to the groin, associated with desire to urinate, nausea and vomiting. The pain lasted five hours. Over the next few days she complained of difficulty in urinating.

The family history disclosed that her mother had been diabetic. She was also a suspected diabetic 17 years prior to admission, but since then she had not shown evidence of diabetes. Her weight was about 190 pounds.

On admission she was found to have a blood pres-

sure of 142/88. The pulse rate was 84 per minute, and the temperature was 99.5 F. The heart was in normal sinus rhythm, with sounds of fair quality; no murmurs were heard. There was some tenderness in the right costovertebral angle. An x-ray film of the chest was within normal limits. The electrocardiogram showed evolutionary changes of a myocardial infarction of the anterior wall. A urinalysis revealed 2+ albumin and 2+ glucose. No red cells were demonstrated.

In view of the possible renal infarction, she was started on dicumarol, and was finally discharged on the thirty-fifth hospital day.

This patient was a suspected diabetic many years prior to admission. Nevertheless, the diagnosis was not proved, although it is possible that she has a latent diabetes. The history clearly reveals that she had a mild myocardial infarction that was followed two days later by probable embolization to her right kidney, with fairly severe manifestations.

*Case 14** H.G. A 60 year old lawyer, 6 feet 2 inches tall and weighing 235½ pounds. For many years he had physical examinations at frequent intervals. He enjoyed excellent health until the present illness. In recent years he had followed a low cholesterol diet.

In March 1955, he experienced shortness of breath on mild exertion, such as walking from his house to his car. He also developed pain in his chest, especially on deep respiration. He sought medical advice and was told that he had virus pneumonia. The symptoms increased. He went to bed and developed a slight fever. After a week in bed he noticed pain in his left calf. He was then told that he had phlebitis and was ordered to stay in bed with hot packs and with the foot of his bed elevated. Suddenly, on April 8, the right leg became cold, white, and numb. The left leg also became cold, but less so than the right. Dr. Foley saw him in consultation at the Lawrence Hospital in Bronxville, New York.

On examination it was found that he was pulseless below the waist. The large and small left superficial saphenous systems were involved in a phlebitic process. It was thought that the patient had suffered a saddle embolus, and that the probable origin of the embolus was from the heart. An electrocardiogram showed an extensive anterolateral infarction. The patient was placed on an oscillating bed and anticoagulants were started. His course was very rough.

Several days later he developed atrial fibrillation. This responded to digitalis therapy. After 3 weeks in bed he was ambulated. From then on his course was excellent. Collateral circulation developed in the legs. The femoral pulse returned to the left groin, but remained absent on the right side. His walking distance had gradually increased, and at present he is able to play nine holes of golf.

When last examined on September 5, 1955, his oscillometric readings were as follows:

	Right	*Left*
Foot	0.3	0.7
Above ankle	2.0	3.5

In retrospect, it appeared that this patient had developed a mild myocardial infarction as the initial phase of his illness. While resting in bed he developed phlebitis and, later, a saddle embolus, which occurred secondary to a mural thrombus in the left side of his heart. The infarction gave such mild symptoms that it was not recognized nor suspected by the physicians attending him.

Discussion

From these case presentations it is clear that all these patients could have been classified initially as "good risk" cases, or mild forms of myocardial infarction. Complete absence of the classical signs and symptoms was characteristic of two cases (7 and 11); in 2 others (1 and 5), the only complaints that could indicate the development of the infarction were represented by mild fatigue and by slight precordial pressure on exertion. Some of the patients (cases 2 and 12) developed symptoms of such a mild nature that their cardiac origin was not recognized at the beginning, and the patients were treated for a while with diathermy and sedatives. In a few, the pain was of moderate or severe intensity, but subsided promptly, either spontaneously or by the effect of morphine. In one case (9), although the pain receded, intermittent precordial discomfort persisted for several hours, and stressed the difficulty of deciding whether symptoms of this sort should be considered as "intractable pain," since there is confusion regarding a proper definition of the term. The importance of this is obvious if one wishes to classify a patient as a "good" or "poor risk" case.

The heart showed some enlargement that we did not consider significant in 4 of our 14 patients. Here again, we have no precise definition of what should be considered "significant enlargement of the heart," one of the points mentioned by Russek in his criteria for classification of patients in "poor" and "good risk" groups.

These 14 so-called "good risk" cases of myo-

* From the Lawrence Hospital, Bronxville, N. Y. Introduced through the courtesy of Dr. William T. Foley.

cardial infarction developed a total of 18 certain and 4 probable thromboembolic complications. Of four patients who sustained silent infarctions, or attacks of such mildness that the symptoms were unrecognized as being of cardiac origin, two (cases 1 and 5) developed thromboembolic complications as the presenting symptom of the clinical picture, and both of them suffered an amputation of a limb.

There were 4 major amputations in 3 patients (cases 1, 4 and 5), one of whom (case 4) finally died after a series of thromboembolic phenomena. One minor amputation was performed in another person (case 2), in whom anticoagulants were used inadequately and for too short a period of time. In this patient, the embolism occurred when she was taken off anticoagulants and her prothrombin time had virtually returned to normal. Six patients (cases 3, 7, 8, 10, 12, and 14) developed arterial insufficiency of the lower extremities as a consequence of embolization to the terminal aorta or peripheral vessels.

Although thromboembolic complications are not frequent in the majority of "good risk" cases of myocardial infarction, they occur occasionally and may lead to disastrous results that can even be fatal, as illustrated by case 4.

As can be seen from the case histories of those patients (cases 7, 8, 9, and 10) who were admitted to the hospital shortly after the myocardial infarction had occurred and before the onset of thromboembolic complications, the absence of serious signs during the first 48 hours of hospitalization did not exclude them from developing thromboembolic complications.

In the past, the question of the risk of hemorrhagic complications from the use of anticoagulants has quite justifiably given rise to concern. This risk has steadily decreased as physicians and technicians have become more familiar with this form of therapy. Severe hemorrhage and rupture of the myocardium have been much more common in serious cases of myocardial infarction. Both these complications have been very rare in mild cases. An important added factor of safety has been the increasing use of Vitamin K_1, which acts within a few hours when administered either orally or parenterally. Ten to 50 mg. of this substance will control most elevated prothrombin-time levels, and the dose may be repeated if necessary. While treatment must be meticulous, the risk of hemorrhage no longer constitutes a serious deterrent, if the indications for anticoagulant therapy are clear.

Conclusions

This and other experience leads us to conclude that serious thromboembolic complications occur in initially mild cases, and that the prognosis in myocardial infarction can never be predicted with certainty during the first 48 hours of hospitalization. It has been demonstrated that anticoagulants markedly reduce the incidence of this type of complication, and we hold that if no contraindications are present, patients of this type should be given the benefit of anticoagulant therapy. It does not appear justified to wait until thromboembolic complications occur, which may be serious, as these cases illustrate, before beginning the administration of anticoagulant therapy.

Summario in Interlingua

Complicationes thrombo-embolic occurre frequentemente post infarcimento myocardial. Le uso de therapia anticoagulante in infarcimento myocardial es generalmente acceptate, sed certe autores ha recommendate abstention ab iste therapia in "leve casos" excepte quando illos disveloppa complicationes thrombo-embolic. Le presente autores opina que isto non es justificate, providite que il non ha altere contraindicationes a providite que le requirite facilitates es disponibile. Es presentate summarios de 14 casos "a prospectos favorabile" de infarcimento myocardial in que il habeva 18 certe e 4 probabile complicationes thromboembolic. Le resultato esseva le necessitate de 4 major amputationes in 3 patientes. Un de illes moriva. Altere complicationes es discutite in detalio.

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Aberrant Ventricular Conduction of Escaped Beats

Preferential and Accessory Pathways in the A-V Junction

By Alfred Pick, M.D.

Escape beats recorded in clinical electrocardiograms sometimes differ in contour and QRS duration from conducted beats, and this in spite of their having a relatively short cycle length. This suggests a location of the subsidiary pacemaker above the bifurcation of the common A-V bundle. While this, unlike other types of aberrant ventricular conduction, cannot be explained on a functional basis, recent investigations on the structure of the normal A-V junction suggest that "paraspecific" A-V connections may act as preferential pathways to the ventricles in some A-V nodal escape beats. Difficulties and guides in differentiating A-V nodal from ventricular escapes under such circumstances are pointed out. On the basis of clinical, electrocardiographic and anatomic facts such a *normal preferential* A-V conduction must be distinguished from an abnormal accessory A-V conduction causing the pre-excitation (Wolff-Parkinson-White) syndrome. However, the two may occur in association.

WHEN consecutive atrial impulses fail to stimulate the ventricles at an appropriate rate, subsidiary, ordinarily subdued, cardiac pacemakers will come into operation. First to escape under such circumstances are centers in the A-V junctional tissues because this area has the ability to create impulses at a rate faster than pacemakers in the ventricles. Centers below the bifurcation of the common bundle will come into action when formation of impulses in the A-V junction is depressed, or conduction to the ventricles of such impulses is prevented by interference or block. It is generally accepted that the distinction between the two types of ectopic beats can be made in the electrocardiogram on the basis of the length of their cycle and the contour of the QRST. Impulses arising in junctional tissues above the bifurcation, in a supraventricular pacemaker, are expected to take over ventricular activation promptly, at rates between 40 and 50, and to produce ventricular complexes resembling beats of atrial origin in all regards. Impulses originating below the bifurcation, in a ventricular pacemaker, appear tardily, at rates of 30 or less, and give rise to aberrant ventricular complexes with prolonged QRS and abnormal ST-T contours.

In the following report several clinical records are presented showing escaped beats during various abnormal rhythms in which the escape origin cannot be easily established on the basis of the above criteria. These are examples selected from many other instances encountered in the course of the past years in routine tracings as well as during the study of simple and complex forms of disturbances of rhythm.[1] Yet, despite this common occurrence, hardly any mention of the problem can be found in the literature.[2, 3] It is the intent of this report: (1) to point out the varieties of contour deviations occurring in escapes of apparently supraventricular origin; (2) to call attention to difficulties and possibilities in determining, under such circumstances, the site of the ectopic subsidiary pacemaker; (3) to attempt an explanation of ventricular aberration in supraventricular escapes by a mechanism which is comparable to, yet different from, that assumed to be in operation in the pre-excitation syndrome.

Material and Methods

The material comprises selected electrocardiograms of 11 different cases in whom escaped beats were recorded as a consequence of various types of

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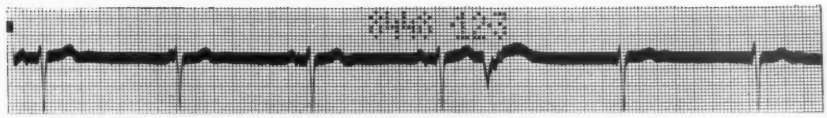

FIG. 1. Typical nodal escapes occurring during sinus bradyarrhythmia, and subsequent to a nodal premature systole with retrograde A-V and aberrant ventricular conduction.

In the first half of the record broad and diphasic P waves are seen indicating irregular and slow (38–46) activity of the sinus node and an abnormal spread of its impulse through the atria. These impulses are conducted to the ventricles at a P-R of 0.20 second, except the second which interferes with one from the A-V node escaping at a cycle length of 1.44 seconds (corresponding to a rate of 42). This nodal beat, apart from the short P-R distance, resembles precisely the conducted sinus beats in contour and QRS duration. The fifth beat of the record is a premature systole of bizarre contour. It is followed by a pause during which a P wave fails to appear at the anticipated time; instead a much earlier, inverted P is seen within the S-T of the premature systole, obviously caused by retrograde spread of the ectopic impulse to the atria. The last two ventricular beats are nodal escapes corresponding in timing and shape to the second beat of the record, and during this time no sign of atrial activity is seen. The sinus node appears to be in a depressed state subsequent to its premature discharge by the retrograde ventricular impulse, but it is possible that retrograde P waves are hidden within the QRS of the two nodal beats.

At first glance, the contour of the premature systole suggests its origin in the ventricles. However, one would expect the subsequent nodal escape interval to be prolonged, as compared to the other escapes, by the retrograde conduction time of the ventricular impulse to the subsidiary A-V nodal pacemaker. Since such prolongation does not occur, it must be concluded that the premature systole takes its origin within, or close to, the point of origin of the escaped beats, that is within the A-V node, and its bizarre contour is caused by aberrant ventricular conduction due to its early appearance in the cycle, when some part of the ventricles is still in a refractory state. The close similarity of sinus and escaping nodal beats on the other hand indicates that both types of impulses use the same pathways in activating the ventricles—as is ordinarily the case.

disturbances of impulse formation or impulse conduction. These records are grouped in figures 1 through 5 according to the type and/or duration of QRS of the ectopic beats. A detailed analysis and interpretation of each tracing is presented in the respective legends and the reasons are there outlined why the origin of the escapes was ascribed to areas above, or below, the bifurcation of the common A-V bundle, or could not be determined. Thus, figure 1 illustrates typical nodal escapes and their close similarity to conducted sinus beats in contrast to aberrant ventricular conduction of a nodal beat occurring prematurely. In figure 2 four cases are reproduced in which a supraventricular origin of the escaped beats was postulated on the basis of their normal QRS duration, in spite of slight or marked differences in contour from that of the conducted supraventricular beats. Figure 3 exemplifies the problem in determining the origin of escaped beats when promptness of their appearance does not conform with a marked contour aberration and a prolonged QRS duration. Identification of a ventricular escape on the basis of the occurrence of ventricular fusion beats is demonstrated in figure 4 in two instances, one of which shows evidence of parasystolic action of the ectopic pacemaker. Finally, in figure 5, a case of ventricular pre-excitation, escaped beats are seen which differ in shape from both the normal and anomalous ventricular complexes and suggest that various pathways to the ventricles may be available to impulses crossing the A-V junctional tissues from above and those arising within them. The physiologic background and new anatomic data to be considered in the explanation of aberrant ventricular conduction of escape beats are pointed out below.

COMMENT

Ordinarily, aberration in the contour of QRST complexes is the electrocardiographic manifestation of the failure of supraventricular impulses, traversing or initiated in the A-V junction, to complete ventricular activation via ordinary conduction pathways because part of these pathways is in a state of partial or complete refractoriness at the time of arrival of the impulse. With normal or slow heart rates this has to be ascribed to an abnormal prolongation of the refractory period, a block, somewhere in the system of the two bundle branches. When aberration of the QRST complexes is limited to beats with a short cycle it may be due entirely to the operation of the normal refractory period in some parts of the conduction system. In about 85 per cent of the beats affected by the

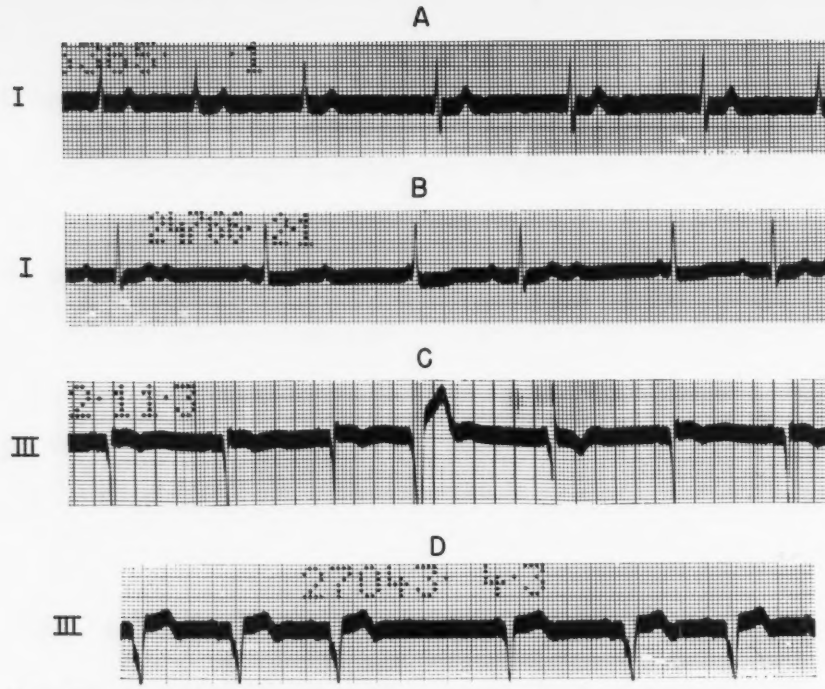

FIG. 2. Escapes with aberrant contour but without QRS prolongation. The four strips are records from different patients.

In *A*, *atrial fibrillation* is present with a slow ventricular rate averaging 55. There are two types of ventricular complexes. The first three and the last, occurring at varying R-R intervals, represent *conducted atrial impulses*. The fourth to sixth beat, with a prominent S wave and a slightly higher T wave have the same R-R interval of 1.24 seconds (corresponding to a rate of 48), the longest of the record. These evidently are *escaped beats*. Their normal QRS of 0.08 second, equal to that of the conducted beats, indicates that they arise above the bifurcation of the common A-V bundle, presumably in the A-V node. Their different contour reveals an anomalous spread of the nodal impulses through the ventricles.

In *B*, similar conditions are present during *sinus rhythm* (rate 86) *with a second degree A-V block*, as in *A*. Again two types of ventricular complexes are seen. One type (the first, fourth and last beats) has a constant relationship to P waves (P-R 0.28 second) and represents *conducted sinus impulses*; the other type differs from the conducted beats in having no S wave, a depressed S-T and a lower T wave. The P-R distance of these beats is shorter and variable in contrast to that of the conducted beats but the R-R interval is constant (1.34 seconds) corresponding to a rate of 45. These are *escaped beats*. Their supraventricular (nodal) origin is evidenced by the normal (0.08 second) QRS duration; however, an anomalous ventricular spread is indicated by the difference in contour as compared with beats of sinus origin.

In *C*, a case with a recent posterior wall infarction, the regular sequence of sinus beats (rate 68, P-R 0.18 second) is disturbed by a *ventricular premature systole* (the fourth beat). The ensuing ventricular pause is less than compensatory and is terminated by a beat (the fifth) occurring shortly (0.08 second) after a P and differing in contour from the conducted beats by a smaller Q, a larger R, and a less elevated S-T and a more inverted T—an *escape beat*. The escape, therefore, originates above the bifurcation of the common bundle, but its impulse spread through the ventricles is altered.

In *D*, a case of intraventricular block (QRS 0.14 second), an *escaped beat* (the fourth QRS) follows a pause engendered by a *nonconducted atrial premature systole*; the premature (inverted) P wave is superimposed on the end of T of the third sinus beat. The ectopic atrial impulse entered and transiently depressed the sinus node as evident from the prolongation of the first sinus cycle following the pause. The escaped beat which interferes with this sinus impulse differs from the conducted beats in having a normal (0.08 second) QRS duration. Its origin cannot be definitely established and two interpretations are possible. It may originate in the A-V node and its normal QRS duration could be attributed to recovery of intraventricular conduction during the ventricular pause. Or it may originate in the ventricular septum below a blocking lesion of one of the bundle branches; under these circumstances its impulse could reach both bundle branches in about the same time and thus cause shortening of QRS in contrast to the supraventricular sinus beats. The first interpretation appears to be the more likely one.

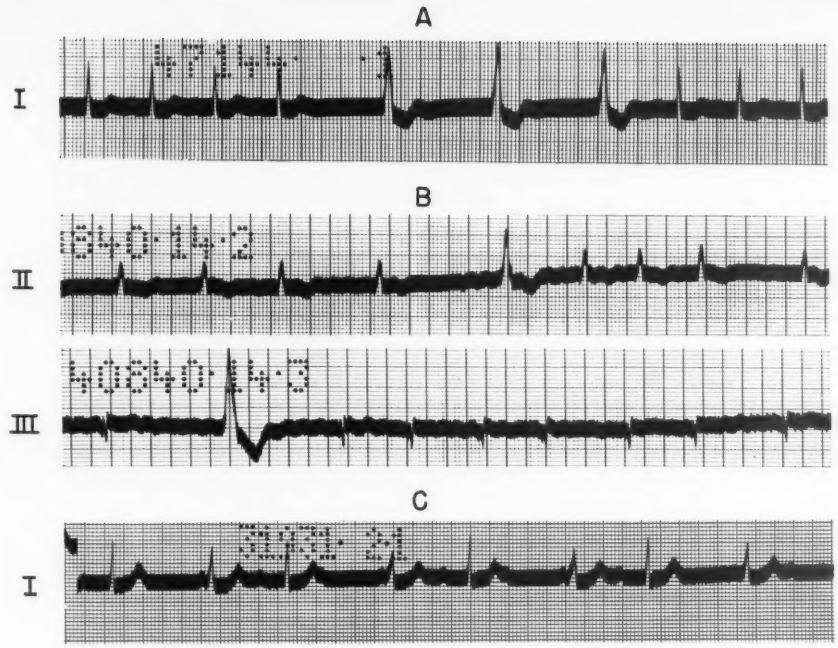

FIG. 3. Escapes with aberrant contour and prolonged QRS complexes. Records obtained on three different patients.

Record *A* starts and ends with a series of regular sinus beats occurring at a rate of 94 and a P-R of 0.24 second. In the middle of the record the P waves disappear and three ventricular beats with prolonged QRS (0.12 second) and an abnormal ST-T contour occur at regular R-R intervals of 1.08 seconds (corresponding to a rate of 56). The last coincides with a sinus P wave reappearing after 3.44 seconds, an interval approaching the duration of five sinus cycles. This suggests the presence of an *intermittent S-A block*. The three aberrant ventricular beats evidently are caused by impulses of a subsidiary pacemaker escaping during the atrial pause.

In *B*, during *atrial fibrillation*, with a ventricular rate averaging 70, in each of the two leads one beat is seen differing from the others in size, shape and QRS duration (0.16 second). Both these beats occur at the same R-R interval of 1.28 seconds, which is the longest of the record. This indicates their ectopic origin in an escaping subsidiary pacemaker.

In *C*, a case of *second degree A-V block*, regular P waves can be spaced throughout at a rate of 100. Of three successive P waves, the first is followed by a QRS at a P-R of 0.30 second, the second is blocked and the third just precedes a QRS at a P-R of 0.08 second. Thus, except at the end of the strip, long ventricular cycles (1.08 seconds) alternate with shorter ones (0.80 second)—a ventricular bigeminy. The ventricular beats are of two types. The one with the shorter R-R (and long P-R) has a slender QRS of 0.06 second duration; the other with the longer R-R (and short P-R) consists of a smaller R wave of 0.10 second duration which is more or less slurred in its upstroke. In both the T wave is upright and of the same size and contour. Superficially, intermittent occurrence of an initially slurred R wave in association with an abnormally short P-R could suggest ventricular pre-excitation (the Wolff-Parkinson-White syndrome), anomalous A-V conduction alternating with A-V conduction over normal pathways at a persistent 3:2 A-V ratio. If this were true, however, one could expect that: (1) variations in the degree of slurring of R in the anomalous beats would be associated with variations in their P-R interval and (2) secondary T-wave changes would result from the operation of the ventricular pre-excitation. Since both these anticipated alterations are absent it appears more likely that the anomalous beats represent escaped beats of a subsidiary pacemaker interfering with the conduction of every third sinus impulse with a resulting 3:1 A-V conduction ratio.

In all three records, QRS prolongation of the escaped beats suggests their origin below the bifurcation of the common A-V bundle. On the other hand the promptness of their appearance, at a rate around 50, is unusual for a true ventricular pacemaker but is common for escapes arising in the A-V junction. In these three instances a distinction between nodal escapes with aberrant conduction and ventricular escapes is not possible (fig. 4).

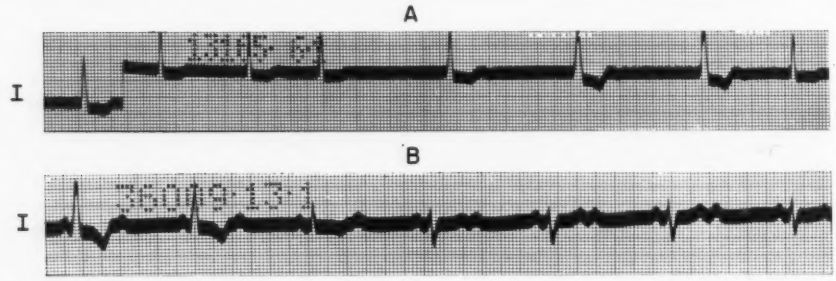

FIG. 4. Escape of a ventricular pacemaker demonstrated by the occurrence of ventricular fusion beats. The two records are from different patients.

In *A*, during *atrial fibrillation*, three types of ventricular beats are seen. The first type, with a strain pattern and QRS of 0.08 second duration (the second to fourth and the last beat), occurs at irregular R-R intervals at an average rate of 70; these are *conducted atrial impulses*. The second type, similar in contour to the first but with QRS prolonged to 0.14 second and the S-T more depressed and T more inverted (the second and third last beat), occurs at a cycle of 1.56 seconds, corresponding to a regular rate of 38; these are *escaped beats* of a subsidiary pacemaker. The third type, intermediate between the first two in QRS duration (0.10 second) and ST-T contour (the first and fifth beat), has the same R-R interval (1.56 seconds) as the second type. These are *ventricular fusion* beats resulting from competition of a conducted atrial and an escaping ectopic impulse in activating the ventricles. The interval separating the two fusion beats is not a multiple of the cycle length of the ectopic pacemaker, ruling out a parasystolic action of the latter.

In *B*, at a regular sinus rate of 95, the fundamental disturbance of rhythm is a *2:1 A-V block*. Again three types of ventricular complexes are seen. The first type with a P-R of 0.16 second and a pattern of right bundle branch system block (QRS 0.12 second) (the fifth and sixth beat) represents *conducted sinus impulses*. The second type, with a pattern of left bundle branch system block and a QRS prolonged to 0.12 second (the first beat) occurs at a foreshortened P-R and represents an *escape* of a subsidiary pacemaker operating at a cycle length of 1.26 seconds, that is at a rate slightly slower than half the sinus rate. The other beats (the second, third and last) resemble in contour one or the other of the two principal types but their QRS and/or T wave is smaller and their QRS duration shorter. These are *ventricular fusion beats* resulting from simultaneous invasion of the ventricles by the two types of impulses. Their variable contour reflects the relative amount of ventricular myocardium activated by each impulse and depends on the time relation of the ectopic impulse to a P wave. Thus, with a P-R distance of less than 0.16 second, ventricular activation is dominated by the ectopic impulse; with a P-R of 0.16 second the sinus impulse succeeds in "capturing" the ventricles to a greater part (or entirely). The interval between the third and the last beat of the record (both fusion beats) is 5.02 seconds, 0.02 second shorter than four times 1.26 seconds, the cycle length of the ectopic pacemaker. Hence, continuous *parasystolic* operation of the subsidiary pacemaker is suggested (which could actually be proven in long strips).

In these two cases, the occurrence of ventricular fusion beats is the evidence for the location of the escaping ectopic pacemaker below the bifurcation of the common bundle. No competition for activation of the ventricles is possible when sinus and ectopic impulses share a common pathway through the A-V junction. In both these instances the aberrant contour of the escaped beats can therefore be ascribed to an origin of the subsidiary impulses within the ventricles.

latter mechanism, a contour characteristic for a right-sided conduction defect develops.[4]

Aberration as encountered in escaped beats and illustrated in figures 2 through 5 does not comply with these criteria. Deviations in their QRST contour cannot be attributed to the action of the normal refractory phase of the conduction system considering the long cycles of these beats. Nor, by the same token, is it possible to invoke a latent abnormal intraventricular conduction defect in all such cases. The operation of the normal or abnormal refractory phase should become manifest in beats of the dominant rhythm rather than in the slow escape beats. Only in figure 2*D* is such an interpretation feasible though another possibility is indicated in the legend. Furthermore, the type of aberrant ventricular complexes in escape beats does not correspond to that encountered in ordinary instances of aberrant ventricular

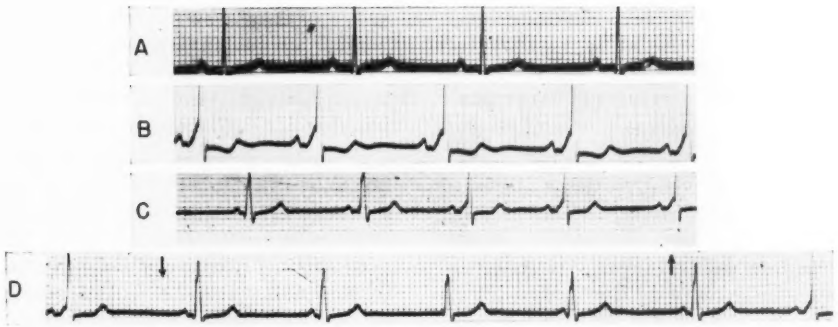

FIG. 5. Escapes with aberrant ventricular conduction in ventricular pre-excitation (the Wolff-Parkinson-White syndrome). The four strips (all lead I) were recorded on different occasions in the same patient. The time lines indicate 0.05 second.

In *A*, at a sinus rate of 51 and a P-R of 0.20 second, ventricular activation and deactivation takes place in a normal fashion as indicated by the slender QRS of 0.08 second duration and the upright T wave. In *B*, at a sinus rate of 60, *ventricular pre-excitation* is evident from the shortening of P-R (0.12 second) in association with the typical change in the QRST contour; a pronounced delta wave prolongs the QRS duration to 0.14 second and causes a secondary S-T depression and partial T inversion. In *C*, the sinus rate varies from 48 to 67 and the last three beats show ventricular pre-excitation as in *B*. The first two differ from both the pre-excitation beats and the normal beats seen in *A*. There is a small Q wave, a notch near the top of R, and QRS measures 0.10 second while the ST-T contour is normal. Their R-R interval (1.27 seconds) is 0.05 second longer than the corresponding P-P interval and hence, their P-R distance differs by the same amount. These are *escaped beats* originating in the A-V node. Their impulses prevent transmission of sinus impulses over normal as well as anomalous A-V pathways with *intermittent A-V dissociation* resulting. In *D*, A-V dissociation was induced by *carotid sinus pressure* (indicated by arrows). The record starts with a pre-excitation beat. As the sinus rate progressively slows to 48, the A-V node escapes at a regular rate of 53 to interfere with five successive sinus impulses. A-V conduction with ventricular pre-excitation is resumed in the last beat following restoration of the sinus rate to 58.

The supraventricular (A-V nodal) origin of the escaped beats is indicated by their normal QRS duration and by the presence of a small "septal" Q wave, like that seen in the normally conducted sinus beats. To account for the difference in contour of these two types of beats some anomalous spread of the nodal impulse in the ventricles must be postulated but differing from that occurring in the pre-excitation beats. It would, therefore, appear that in this case ventricular activation can take place in three different ways: (1) entirely over *ordinary* A-V conduction pathways, resulting in beats with a normal P-R interval and QRST contour; (2) over an *accessory* A-V path, resulting in beats with shortened P-R and pre-excitation contour and (3) over some *preferential* path, limited to impulses originating in the A-V node and resulting in beats with slight QRS aberration.

conduction. When the QRS of escaped beats is abnormally prolonged and associated with secondary ST-T alterations, the assumption of a supraventricular origin rests entirely on the promptness of their appearance (fig. 3*A* and *B*). However, when both the QRS duration and ST-T contour are normal, as in figure 2, their origin above the bifurcation of the common bundle is almost certain.

There are other possibilities to be considered in an attempt to account for an aberrant contour of escaped beats. Thus, alterations in the shape of supraventricular beats are known to occur subsequent to longer ventricular pauses engendered by premature systoles, by a second degree A-V block, or occurring in atrial fibrillation and flutter.[5-7] However, this type of alteration, the cause of which is obscure,[8] involves mainly the contour of the T wave and usually is restricted to the first beat after the pause. Where the phenomenon continues for several cycles an alternation of the T wave contour may be seen before it resumes its original appearance.[1, 9] Contrariwise, in escaped beats the aberration involves primarily the QRS contour while the T wave may remain completely unaltered, and this is maintained in consecutive escapes. Normalization of the ven-

tricular complex takes place abruptly, with the reappearance of the dominant rhythm. Another rare mechanism could be the operation of a supernormal phase of intraventricular conduction.[10] This may perhaps apply to some specific cases but cannot generally account for a phenomenon occurring so commonly.

While, therefore, in the light of known normal and abnormal cardiac physiology, it seems impossible to explain an aberrant contour of supraventricular escapes on a functional basis, anatomic background for a feasible interpretation has been provided by recent investigations on the structure of the specific conduction system in the mammalian and human heart. The stimulus for the resumption of such studies were the doubts expressed by some workers concerning the existence of a specific conducting system on the one hand, and the unsolved problem of ventricular pre-excitation on the other. The latest authoritative review of the subject by Lev, and his own careful investigations,[11] leave no doubt about the validity of our present concepts concerning a specific muscle system joining atria and ventricles. But his studies also led to the recognition in normal fetal, newborn and young adult human hearts of irregular communications of the A-V node, the common A-V bundle and the beginning of the left bundle branch with ordinary ventricular myocardium, a confirmation of "paraspecific fibers" described previously by Mahaim[12] and by others.[13, 14] The demonstration of these additional muscle bridges in the normal heart may in the future necessitate some revision of present views concerning the order of ventricular activation provided it could be proved that these fibers have a function of conductivity, a very difficult task.

But supposing that paraspecific fibers, like ordinary specific fibers, do have the potential property of transmitting impulses, their topical relation to nodal tissue could serve very well as a clue for certain hitherto unexplained observations in clinical electrocardiograms and, in particular, the phenomenon discussed in this report, namely, aberration of QRST limited to impulses initiated by nodal or infranodal structures. Confronting electrocardiographic facts, as illustrated in figures 1, 2, 3 and 5, with these recently established histologic data, a hypothesis can be developed to account for the occurrence of normal intraventricular conduction of A-V nodal impulses in some, and more or less aberrant conduction in other instances. All that is required is the assumption that impulses arising in peripheral portions of A-V junctional tissue, in the vicinity of the point of origin of paraspecific fibers, reach part of the ventricular myocardium over *preferential* (paraspecific) pathways[2] in contrast to impulses arising more centrally in the A-V junction and traveling to the ventricles over ordinary paths, like supranodal impulses (fig. 1). Depending on the length, the course, and the point of insertion of such preferential pathways, and especially their nearness to the ordinary A-V junction, the contour aberration of the resulting ectopic ventricular complex would be more or less pronounced and would vary from case to case (figs. 2, 3 and 5).

Conceivably such preferential pathways could operate even in the absence of paraspecific fibers if one assumes that the arrangement of conducting fibers in the lower A-V node and common A-V bundle is such as to determine impulse distribution to specific limited parts of the ventricular myocardium—an arrangement comparable to that of the internal capsule of the brain. Prinzmetal and associates[15] have postulated this to support their concept of "accelerated A-V conduction." Implication of the latter in the case of nodal escapes is unnecessary, since impulses initiated in distal parts of the A-V junction and proceeding over preferential pathways at a *normal speed* could reach one ventricle earlier than the other and thus cause aberrant ventricular complexes, in contrast to impulses arising higher up and distributed simultaneously to both ventricles.

Evidently, if this concept is correct, present criteria for location of the origin of escape beats, whether above or below the bifurcation of the common A-V bundle, would require amendments and amplifications. Difficulties will arise in particular when escapes are encountered conforming to idioventricular beats in QRST contour but not in timing (fig. 3). In such cases a retrograde P wave preceding the beats under question would favor their nodal origin. But

this is seen only rarely in escaped beats[16] and cannot be expected in atrial fibrillation or in the presence of A-V block, the two conditions in which escape of subsidiary centers is encountered most commonly. As another point of distinction, foreshortening of the first ectopic R-R cycle may be used—since this occurs at the onset of nodal rhythms in contrast to idioventricular rhythms. But this criterion becomes applicable only if escapes are repetitive (revealing the true nodal interval) and is not observed invariably in nodal rhythms; in fact depression of nodal activity by preceding (conducted) impulses[17] may counteract the apparent abbreviation of, and even prolong, the first R-R in nodal rhythm. The most reliable criterion of an idioventricular origin of escapes is the finding of ventricular fusion beats (fig. 4), a principle also valuable in the identification of ventricular paroxysmal tachycardia.[18] Obviously, when two simultaneous heterogenetic impulses share the activation of the ventricles at least one must have been initiated beyond the bifurcation of the common A-V bundle.

If the concept of functioning short-cuts between A-V junctional structures and the ventricular myocardium should turn out to be valid, then such *normal preferential* pathways operating in nodal escape beats must be distinguished from *abnormal accessory* pathways operating in the pre-excitation (Wolff-Parkinson-White) syndrome. Data have been presented in a recent report from this department[19] which strongly favor the latter mechanism against all other invoked in the search for the cause of ventricular pre-excitation. There are several reasons to distinguish the two conditions. Aberrant conduction of escaped beats is common in clinical electrocardiography and bears no relation to the incidence of paroxysmal supraventricular tachycardia in contrast to the pre-excitation syndrome. Furthermore, pre-excitation beats typically reveal a distinct "anomalous component," the delta wave, and secondary ST-T alterations, in contrast to aberrant supraventricular escapes. This is well demonstrated in figure 5, where both types of beats occur side by side. In most instances, the electrocardiographic pattern will permit the differential diagnosis but difficulties may arise when the type of QRS aberration in escape beats imitates the delta wave of ventricular pre-excitation (fig. 3*C*).

There is also reasonable anatomic background for a hypothesis ascribing the two types of aberration of ventricular complexes to two different types of anomalous A-V conduction pathways. Paraspecific fibers have been described as originating in the A-V node and proximal parts of the specific conduction system, and as maintaining a course close to ordinary conduction pathways. Accessory muscular A-V bridges, on the other hand, demonstrated in a few completely and carefully examined cases with ventricular pre-excitation, were found remote from the A-V junction, bypassing the A-V node. Supposing that both types of fibers have the function of conductivity, one might expect that nodal impulses entering preferential, and perhaps soon rejoining ordinary pathways in the ventricular septum, should produce comparatively little alterations of the ventricular complex in the electrocardiogram compared with pre-excitation beats. In the latter, supraventricular impulses traveling over abnormal accessory A-V connections would directly reach ventricular myocardium of the free walls and hence cause profound alterations in the sequence of ventricular activation and deactivation. Conceivably normal preferential and abnormal accessory pathways could be in action in the same case as is suggested by the observation reproduced in figure 5.

Summary and Conclusions

(1) An aberrant QRST contour of escape beats is commonly encountered in clinical electrocardiography. Selected examples are presented, illustrating the problems of locating the subsidiary pacemaker above or below the bifurcation of the common bundle under such circumstances.

(2) Present criteria based on QRS duration and time of appearance of the escapes may be unreliable in the differential diagnosis of supraventricular and ventricular subsidiary pacemakers. The latter can be diagnosed with certainty when ventricular fusion beats are recorded.

(3) Aberrant conduction of supraventricular (nodal) escapes cannot be accounted for on a functional basis. However, a background for a feasible interpretation is provided by recent histologic studies of the A-V junction in the human heart. Paraspecific A-V connections have been demonstrated which conceivably could represent preferential pathways for impulses initiated in proximal portions of the specific system, in particular in the A-V node.

(4) On the basis of clinical, electrocardiographic and anatomic facts, aberrant intraventricular conduction, supposedly effected by the operation of such normal preferential A-V conduction pathways, must be distinguished from the mechanism of ventricular pre-excitation. The latter is to be ascribed to abnormal accessory A-V bridges bypassing the A-V node. However, the two mechanisms need not be mutually exclusive.

(5) The presented concept of preferential A-V conduction is hypothetical and needs experimental or other confirmation.

Summario in Interlingua

(1) Un aberrante contorno QRST de pulsos escappate es de occurrentia commun in electrocardiographia clinic. Es presentate exemplos seligite. Istos illustra le problemas del localisation de centros subsidiari supra o infra le bifurcation del fasce commun.

(2) Le disponibile criterios, que es basate super le duration de QRS e le tempore quando le pulsos escappate se manifesta, non es semper digne de confidentia in le diagnose differential de centros subsidiari supraventricular e ventricular. In casos del registration de pulsos fusional ventricular, le diagnose de centros subsidiari ventricular pote esser diagnosticate con securitate.

(3) Le conduction aberrante de supraventricular (nodal) pulsos escappate non es explicabile super un base functional. Tamen, le base de un plausibile interpretation es providite per recente studios histologic del junction atrio-ventricular in le corde human. Paraspecific connexiones atrio-ventricular esseva demonstrate le quales poteva representar vias preferential pro impulsos initiate in portiones proximal del systema specific, particularmente in le nodo atrio-ventricular.

(4) Super le base de factos clinic, electrocardiographic, e anatomic, le aberrante conduction intraventricular (supponitemente afficite per le functionamento de tal normal vias preferential de conduction atrio-ventricular) debe esser distinguite ab le mechanismo de pre-excitation ventricular. Iste ultime mechanismo es a ascriber a anormal pontes accessori atrio-ventricular que non passa per le nodo atrio-ventricular. Sed le duo mechanismos non se exclude mutualmente.

(5) Le hic-presentate concepto del conduction atrio-ventricular preferential es hypothetic e require confirmationes experimental o altere.

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A Comparative Study of Myocardial Infarction in the White and Negro Races

By PHILIP G. KEIL, M.D., AND LEON V. MCVAY, JR., M.D.

A review of 519 consecutive cases of myocardial infarction reveals an unexpectedly high incidence in the Negro female. Not only does this catastrophe occur at an earlier age in the Negro woman, but also is less frequently associated with angina, pursues a more virulent course and is associated with a higher fatality rate than that recorded in the white race and in the Negro male. Comparative clinical features in the two sexes of the white and Negro races are presented.

A REVIEW of the current literature reflects the widespread and increasing interest in coronary artery disease. In spite of intensive investigation during the past 2 decades, its etiology is still unknown.[1] Despite the encouraging observation that coronary atherosclerosis is a disease and not merely the result of aging,[1-3] prevention or effective treatment cannot be anticipated until the pathogenesis of this condition is understood.

While such possibilities as heredity, diet, hypertension, obesity, diabetes and anatomic factors have been investigated, basic research dealing with atherosclerosis has been largely influenced by the striking difference in sex incidence. The greater frequency in males as compared to females has been reported to vary from 2:1 to 6:1.[4, 5] Perhaps the most significant ratio was reported by White[6, 7] in two separate groups of 100 patients, all under the age of 40 years, with coronary heart disease. In the first group were 96 males and 4 females; in the second, 97 males and 3 females. In attempting to clarify the cause of coronary atherosclerosis, Dock[8] also emphasized the sex difference. Many investigators have suggested that an ovarian hormone may be responsible for the protection of women, especially those under the age of the menopause.[9-12] In accord with this concept, Katz and his associates[13] demonstrated the regression of coronary atherosclerosis in cholesterol-fed chicks following the administration of estrogen. Barr[14] advanced the hormonal hypothesis still further by showing that the administration of estrogen to survivors of myocardial infarction can correct the lipid pattern in the plasma toward that observed in so-called normal individuals. However, an attempt by Oliver and Boyd[15] to treat 10 men having coronary artery disease with estrogenic substances produced no decrease in the incidence and severity of effort-pain or breathlessness. In addition, numerous untoward side effects were noted.

None of the investigations into the etiology of coronary artery disease and its occurrence in females has considered the Negro race separately. In a previous communication we reported the results of a study of 330 cases of proved myocardial infarctions; 162 were white and 168 were Negroid.[16] While the Caucasian males outnumbered the females 3:1, there was no sex difference among the Negroes. In the present paper we expand the size of this series and attempt to analyze the cases in a more comprehensive manner.

OBSERVATIONS

The clinical records of 519 cases of proved myocardial infarction were reviewed. All of the patients receiving this diagnosis over an 8-year period (Jan. 1, 1947, through Dec. 1, 1954) in a large mid-southern university hospital were included. In each instance the diagnosis was established by the clinical findings and was substantiated by characteristic electrocardiographic changes or necropsy findings. The ratio of admissions to the hospital during this period

From the 3810th United States Air Force Hospital, Maxwell Air Force Base, Alabama.

TABLE 1.—*Incidence of 519 Myocardial Infarctions by Decades*

Decades	White Males	White Females	Negro Males	Negro Females
3	0	0	1	1
4	5	0	8	7
5	20	4	23	35
6	42	9	41	38
7	50	19	41	26
8	47	25	37	17
9	9	3	5	4
10	0	0	2	0
	173	60	158	128

was approximately 70 per cent Negro and 30 per cent white; the number of males and females within each race was essentially equal.

Incidence

Of the 519 patients hospitalized because of myocardial infarction, 233 were white and 286 were Negroes (fig. 1). The sex ratio in whites was 2.9:1 and in Negroes 1.2:1. The incidence of myocardial infarction among the Negroes was 52 per cent of that among the white patients.

Age

The average age at the time of the initial myocardial infarction was as follows: white males, 62 years; white females, 66.5 years; Negro males, 60.6 years; Negro females, 56 years. These findings are represented by decades in table 1. It is apparent that the Negro female was stricken at a significantly earlier age than any of the other three groups. This is in direct variance to the classical description

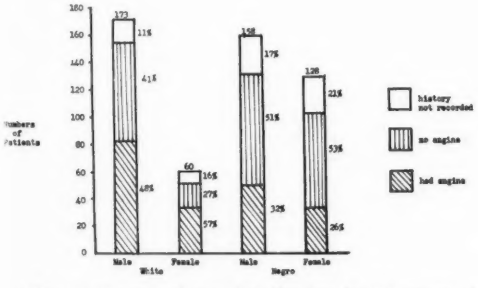

FIG. 1. Race and sex distribution in 519 cases of myocardial infarction.

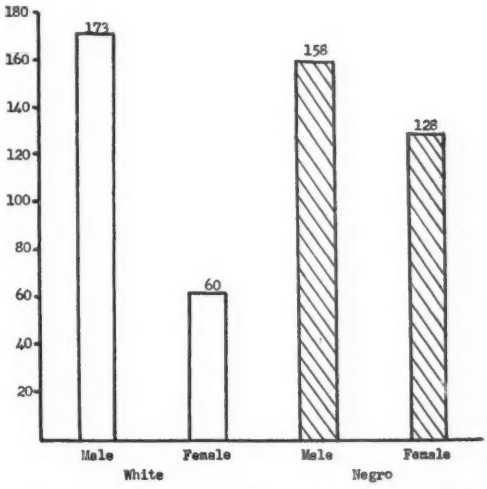

FIG. 2. History of angina by sex and race in 519 cases of myocardial infarction.

of coronary atherosclerosis. Only 4 white females (6.6 per cent) suffered an infarction prior to the fiftieth year of life, whereas 43 (33.6 per cent) of the Negro females had been afflicted by the end of the fifth decade. Before the age of 60, only 13 (22 per cent) of white females were afflicted, as contrasted to 81 (63 per cent) of Negro females. No such pronounced difference was apparent among the males.

Angina

The history of each case was thoroughly reviewed as to the presence of angina pectoris prior to infarction. Chest pain that appeared two weeks or less before infarction was considered to be premonitory and was not included in the analysis. The results are recorded in figure 2. Angina occurred with considerably greater frequency among members of the white race. More than twice as many white females (57 per cent) as Negro females (26 per cent) experienced this distressing symptom and one and one-half times as many white as Negro males.

Body Build

A determination of body build was based on height, weight, and age, according to the method of Duncan.[17] Females were inclined to

be obese, while males were of average size. There was no significant racial difference; 48 (28 per cent) of white males were obese; 91 (53 per cent) were average; 23 (13 per cent) were under weight, and no adequate record was available in 11 (6 per cent). A study of the white female cases revealed that 36 (60 per cent) were obese, 17 (28 per cent) were average, 4 (7 per cent) were under weight, and in 3 (5 per cent) there was no record in the chart. Among the Negro males, 42 (27 per cent) were obese, 91 (58 per cent) were average, 14 (8 per cent) were below average, and in 11 (7 per cent) no information concerning body build was available. Of the Negro females, 76 (59 per cent) were obese, 38 (30 per cent) were within average limits, 5 (4 per cent) were under average size, and in 9 (7 per cent) there was no adequate description.

Blood Pressure

No racial nor sex differences of significance were apparent on analysis on the history of hypertension, though the females of both races were somewhat more inclined to be hypertensive. A consideration of the white males disclosed that 83 (48 per cent) had a history of hypertension, 78 (45 per cent) were normotensive, and in 12 (7 per cent) there was no adequate record. Among the white females 40 (66 per cent) were hypertensive, 19 (32 per cent) were normotensive, and in 1 (2 per cent) this information was lacking. Of the Negro males, 93 (58 per cent) were hypertensive, 52 (33 per cent) were normotensive, and in 13 (9 per cent) this was not adequately recorded. In the group of Negro females, 85 (66 per cent) were hypertensive, 32 (25 per cent) were normotensive and in 11 cases (9 per cent) this information was not recorded.

Family History of Cardiovascular Disease

A history of significant cardiovascular disease in the immediate family was obtained with approximately the same degree of frequency in each sex and race. The large number of charts in which this was not adequately recorded tends to invalidate the importance of this clinical feature in the present study.

Habits

A detailed dietary history was not available in every case. However, all of the patients of both races came from a similar economic level, and in the over-all picture, dietary habits were believed to have no influence on occurrence rates. The role of alcohol and tobacco was considered. Although the use of these agents was not mentioned in a large percentage of records, the figures are of interest. Of the white males, 85 (49 per cent) used tobacco, 10 (6 per cent) were nonsmokers, and no information was obtainable for 78 (45 per cent). Among the white females, 7 (12 per cent) used tobacco, 13 (22 per cent) did not, and in 40 (66 per cent) cases this was not recorded. In the group of Negro males, 73 (46 per cent) used tobacco, 14 (8 per cent) did not, and in 71 (46 per cent) instances this was not known. The charts of the Negro females disclosed that 33 (26 per cent) used tobacco in some form, 23 (18 per cent) did not, and there were no records available in 72 (56 per cent).

With regard to the use of alcohol, the males predominated without a significant racial difference being observed. Among the white males, 20 (12 per cent) were heavy drinkers, 48 (28 per cent) were moderate drinkers, 34 (20 per cent) did not drink, and no adequate history was reported in 71 (40 per cent). A review of the histories of the white females revealed that 3 (5 per cent) used alcohol, 17 (28 per cent) were nondrinkers, and in 40 (67 per cent) this was unknown. In the series of Negro males, 11 (6 per cent) were heavy drinkers, 36 (23 per cent) used alcohol moderately, 26 (16 per cent) were nondrinkers, and in 85 (55 per cent) no adequate history was obtained. Of the Negro females, 17 (13 per cent) ingested alcohol in moderation, 39 (30 per cent) did not drink, while in 72 (57 per cent) this was unknown.

Associated Disease

No particular pattern of associated disease was found. Diabetes mellitus was much more common among the females of both races. The incidence in the women patients, both white

and Negro, was significantly greater than that usually reported in the general population.[18] The appearance of malignancy, particularly that type involving the generative organs, was not found in predominance in either race or sex. Six (3.5 per cent) white males had diabetes and 5 (2.9 per cent) had malignancy; 9 (15 per cent) white females were diabetic, and 6 (10 per cent) had malignancy; 9 (5.1 per cent) Negro males had diabetes and 5 (3.2 per cent) had malignancy; of the Negro females, 20 (15.6 per cent) had diabetes and 5 (3.9 per cent) had malignancy.

Multiple Infarctions

The occurrence of more than one infarct did not explain the high mortality rate in this series of patients. Relatively few had a second infarction. The great majority died with, or as a result of, the first attack. Twenty-two (13 per cent) white males, 3 (5 per cent) white females, 8 (5 per cent) Nergo males, and 7 (5 per cent) Negro females had two or more infarctions.

Deaths

The over-all mortality rate in this series of 519 cases of myocardial infarction was 67 per cent. A further analysis disclosed that of 173 white males 107 (62 per cent) died. Of 60 white females, 44 (73 per cent) died. Of 158 Negro males, 98 (62 per cent) expired and of 128 Negro females, 99 (77 per cent) died. The greatest percentage of deaths, therefore, occurred among the Negro females. This finding is definitely different from that recorded in the literature and in textbooks of medicine.[19, 20]

Female Productivity

Negro and white females had an almost identical history of productivity. Most had more than one child and about half had numerous children. Of the white females, 33 (53 per cent) had children with 20 having multiple pregnancies, 3 (5 per cent) had no children, and no history was recorded for 25 (42 per cent). Among the Negro females, 87 (55 per cent) had children with 55 having multiple pregnancies, 7 (4 per cent) were childless, and in 34 (41 per cent) this was unknown.

Female Pelvic Disease and Surgery

Of the 60 white females, 2 had been subjected to hysterectomy and 1 presented a history of bilateral oophorectomy during the child-bearing years. Of the 128 Negro females, 18 reported a hysterectomy; 4, a bilateral oophorectomy; 3, a unilateral oophorectomy; and 1, a radiation menopause during the child-bearing years. Three of the eight Negro females who suffered a myocardial infarction under the age of 40 years had a previous history of toxemia of pregnancy; this was true of the youngest Negro female (21 years of age) included in this study.

Discussion

Because of certain interesting observations on the incidence of myocardial infarction in Negroes reported in a previous paper, we decided to compare this disease in white and Negro patients.[21] In a series of 330 cases no difference in sex incidence among Negroes was observed; indeed, myocardial infarction appeared to occur earlier and to be more severe among Negro females.[16]

Therefore, it was decided to expand the size of this study and analyze each case in greater detail. In the present investigation 519 cases of proved myocardial infarction were reviewed. During the interval covered by this study 70 per cent of hospital admissions were Negro and 30 per cent were white. The number of males and females within each race was essentially equal. There were 233 white patients, of whom 173 were males and 60 were females. This represents a sex ratio of 2.9 to 1 and is in general accord with the figure accepted in the literature.[22] Of 286 Negro cases, however, 158 were males and 128 were females. This ratio of males to females is only 1.2 to 1 and differs with high statistical significance from the sex ratio in whites. It is important to note that in the many studies dealing with the sex incidence of coronary artery disease the Negro race has never been specifically considered. In the present series the incidence of myocardial

infarction in the Negro was approximately 52 per cent of that in the Caucasian.

A review of the age of all patients at the time of initial infarction revealed a further striking deviation from the classical picture described in coronary artery disease. The rarity of myocardial infarction in females, and especially in those of the younger age groups has been regarded to be quite valuable in the differential diagnosis of chest pain.[23] In a recent review of the literature, Thomas and Cohen[24] found it generally accepted that myocardial infarction may occur in a few young men under the age of 40 but is extremely rare among young women of this age. They cited current reports confirming the following widely held views: (1) that there is a sharp increase in the incidence of coronary atherosclerosis between the ages of 30 and 49 in men and between the ages of 50 and 69 in women and (2), that the incidence of marked coronary atherosclerosis in necropsy studies reaches a maximum between 50 and 59 years of age in men, whereas in women, a plateau is reached after the seventh decade.[25, 26] Clinically, the initial appearance of myocardial infarction is said to occur most often between the ages of 56 and 60; in a recent study, however, 39 per cent of cases sustained the initial attack after the sixtieth year.[27, 28] In the present study, only four white females (6.6 per cent) suffered an infarction prior to the fiftieth year of life, yet this occurred in 43 (33.6 per cent) of the Negro women. Before the age of 60, 81 Negro females (63 per cent) had suffered a myocardial infarction as contrasted to only 13 (22 per cent) of white females. While the observations in this series concerning white females, white males, and Negro males are in complete accord with those generally accepted, this is not true of the Negro females. Infarction actually occurred earlier in the Negro female than in any other category, even earlier than in the white male.

The 519 cases included in this study were analyzed with regard to the incidence of angina prior to infarction. It is generally stated that angina pectoris occurs with equal frequency in both sexes.[22] In the present study this symptom occurred in similar proportions. A striking deviation from the accepted norm, however, was the fact that angina occurred more than twice as frequently in white as in Negro females. This unusual incidence remains to be explained.

The present investigation confirmed the observation that females having coronary artery disease tend to be more obese than do men afflicted with this condition.[24] No significant racial difference was noted. Similarly, hypertension was found to occur more frequently in the females of both races than in the males. This has been well established, and no racial deviation was observed. An analysis of the frequency of a familial history of cardiovascular disease merely confirmed well-documented views. It was not possible to evaluate adequately the role of tobacco or alcohol in this study because of the large number of records not mentioning these agents. It became obvious, however, that all of the patients included in this series were from a similar economic level. No important differences in dietary habits were noted. Laboratory reports dealing with anemia were comparable in both races.

The incidence of diabetes mellitus was similar in the males and in the females of both races. This metabolic disease occurred in 3.5 per cent of white males, 5.1 per cent of Negro males, 15 per cent of white females, and 15.6 per cent of Negro females. The figures dealing with the males of both races are compatible with those usually accepted for the general population: 2.4 per cent among persons 45 to 64 years of age and 5.8 per cent among those 65 years and over.[18] The surprisingly high incidence of diabetes among the females of both races is not readily explained. From the standpoint of the present paper, however, the remarkably close correlation between the white and Negro women eliminates this disease as a factor in the atypical picture of myocardial infarction in Negro females.

Because of the startling absence of the usual sex incidence of myocardial infarction in Negroes, it was considered that ovarian dysfunction might be involved. However, no significant difference in productivity was observed between white and Negro females. It should be noted that 42 per cent of the white

cases and 41 per cent of the Negroes could not be properly evaluated because of inadequate records. Of possible significance was the observation that pelvic surgery during the child-bearing period was performed on 20.3 per cent of the Negro females as contrasted with only 5 per cent of the white cases, a ratio of 4:1. The importance of this finding remains to be determined.

The mortality rate in the present study was greatest among the Negro females. This again is a startling deviation from the classical description of myocardial infarction in women. It would almost appear that coronary atherosclerosis is a different disease in the Negro female as compared with that described in the literature. The explanation of this variation presents a definite challenge. Further extensive study of the Negro female is essential and may well afford an insight into the pathogenesis of coronary artery disease.

Summary and Conclusions

1. The records of 519 cases of proved myocardial infarction were reviewed. Of these patients 233 were white; 286 were Negro. The ratio of hospital admissions was 70:30 in favor of the Negro. The incidence of myocardial infarction in Negroes was 52 per cent of that in Caucasians.

2. The classical sex predominance of myocardial infarction in males was not present in the Negro patients. The ratio of Negro males to females was approximately 1:1 (1.2:1), while among the white patients it was 3:1 (2.9:1).

3. The average age at the time of initial myocardial infarction was 66.5 years for white females, 62 years for white males, 60.6 years for Negro males, and 56 years for Negro females. Infarction occurred, therefore, more than 10 years earlier among the Negro females than among white females. This is a significant difference.

4. A history of angina pectoris prior to myocardial infarction was obtained in 57 per cent of white females, 48 per cent of white males, 32 per cent of Negro males and 26 per cent of Negro females. Angina, therefore, occurred more than twice as frequently among white as among Negro females. This is a significant difference.

5. The highest mortality rate in the present study occurred among the Negro females (77 per cent).

6. Four times as many Negro as white females reported a history of pelvic surgery during the child-bearing years.

7. All cases were analyzed with regard to obesity, diabetes mellitus, hypertension, and family history of cardiovascular disease. No significant racial variation was observed.

8. Myocardial infarction in the Negro female deviated significantly from the classical description of this disease.

9. Further investigation of coronary artery disease in the Negro female is essential and may provide basic information concerning the pathogenesis of this disease.

Summario in Interlingua

Esseva revidite 519 casos consecutive de infarcimento myocardial. Le revista revela un inexpectatemente alte frequentia del morbo in femininas negre. Iste catastrophe occurre in femininas negre a un etate minus matur, e in plus illo es associate minus frequentemente con angina, seque un curso plus virulente, e es associate con un plus alte mortalitate que illo observate in le racia blanc e in masculos negre. Es presentate comparationes del characteristicas clinic in le duo sexos e racias.

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Dilatation of the Pulmonary Artery in Pulmonary Stenosis

By F. S. P. VAN BUCHEM, M.D.

Dilatation of the pulmonary artery occurs frequently in cases of valvular pulmonary stenosis and is often called "poststenotic." We determined the diameter of the pulmonary artery angiocardiographically and compared this with the data obtained by heart catheterization in cases of pulmonary stenosis and of idiopathic dilatation of the pulmonary artery. Features are presented which constitute arguments in favor of Laubry's suggestion that we are dealing with two different abnormalities, namely, a valvular stenosis and a dilatation of the pulmonary artery though hydraulic forces may contribute to the final development of the dilatation.

DILATATION of the pulmonary artery is observed in the majority of cases of pure valvular pulmonary stenosis. This dilatation is often called poststenotic, on the assumption that it results from the stenosis. It is thought that whirls are formed in the blood flow distal to the stenosis, which cause the dilatation. The investigation of Cavina,[2] who succeeded in producing pulmonary stenosis in rabbits, is sometimes referred to in support of this hypothesis. In these experiments, a dilatation of the pulmonary artery was also repeatedly brought about. Histologic examination of the wall of the pulmonary artery, however, led Cavina to the conclusion that the dilatation was due to the disturbed nutrition of the pulmonary arterial wall, since the vasa vasorum were also occluded by the silk thread applied around the pulmonary artery to produce the stenosis. Cavina has emphatically pointed out that, in his opinion, the stenosis itself cannot be regarded as the causative factor. Halsted,[6] who observed the development of "a mild dilatation distal to partial ligation of the terminal aorta," also stated that "it is not denied that the paralysis of the vasomotor nerves and the occlusion of the vasa vasorum may possibly play some part in the manifestation". Recently, Holman[7] has expressed the opinion that the dilatation of the pulmonary artery is the result of the stenosis; he based this opinion upon experiments using elastic rubber tubing.

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We propose to report some clinical findings which, in our opinion, are difficult to reconcile with the conclusion of Holman and also of others.

METHOD

The diameter of the pulmonary artery was determined in patients with various degrees of pure pulmonary stenosis. In order to judge the size of the pulmonary artery, as a rule the degree of prominence of the pulmonary arch in x-ray films or during screening in the frontal and oblique positions, is usually considered. This method can be shown to be quite crude and inaccurate, if the degree of prominence of the pulmonary arch is compared with the diameter obtained from angiocardiograms in the left position. In technically correct angiocardiograms the diameter of the pulmonary artery can be measured. Even though this is not the exact diameter (it is slightly enlarged due to the divergence of the rays), comparable values may be obtained in this way. There are also slight differences resulting from the phase of the cardiac action (diastole and systole). Patients without cardiac abnormalities had an angiocardiographically measured diameter of 22 to 33 mm. In three cases in which the pulmonary arch was found to be only slightly prominent in ordinary films, we found a diameter of 62, 50 and 63 mm., respectively, in angiocardiograms. In all patients cardiac catheterization was carried out in addition; the pressure and oxygen saturation were determined in superior vena cava, right atrium, right ventricle and pulmonary artery (table 1). The values found by these studies were within normal limits in all cases, as was the arterial oxygen saturation. The same studies were done in patients with idiopathic dilatation of the pulmonary artery. In these cases no other abnormalities were found and the systolic pressure in right ventricle and pulmonary artery was the same (table 2).

Results

There was no difference in the configuration of the dilatation accompanying pulmonary stenosis and idiopathic dilatation of the pulmonary artery. In both varieties of dilated pulmonary artery the dilatation has been sometimes saccular (fig. 1), but generally fusiform, with a sharp limitation; usually it has been confined to the trunk of the pulmonary artery (fig. 2). Occasionally one of the two main branches, especially the left, also was dilated, but in no case were the peripheral branches enlarged, the lung fields often being remarkably clear. In uncomplicated pulmonary stenosis no expansile hilar pulsations were observed.

In the various patients with pure pulmonary stenosis the degree of dilatation varied widely, and in some patients no dilatation was present (fig. 3). There was no correlation between the age of the patients and the differences in dilatation (fig. 4).

Comparison of the degree of the dilatation with the pressure in the right ventricle and pulmonary artery, did not reveal any correlation between these values (table 1, fig. 4). For example, diameters of 30 and 73 mm. were observed in two patients who had the same difference in pressure between right ventricle and pulmonary artery (figs. 3 and 5). Similarly diameters of 41 and 63 mm. were found in two

Fig. 1. Gr., age 14. Angiocardiogram made at three seconds. Saccular dilatation of pulmonary artery. Pressure right ventricle, 125/0; pulmonary artery, 23/10; diameter of pulmonary artery, 51 mm.

Fig. 2. H. H., age 23. Angiocardiogram made at 2.5 seconds. Dilatation confined to trunk of pulmonary artery. Pressure right ventricle, 40/0; pulmonary artery, 20/5. Diameter of pulmonary artery, 71 mm.

Fig. 3. P. S., age 16, angiocardiogram made at 2.5 seconds. No dilatation of pulmonary artery. Pressure right ventricle, 34/2; pulmonary artery, 17/7. Diameter of pulmonary artery, 30 mm.

patients with the same systolic pressure in the right ventricle (figs. 6 and 7). Differences in diameter were also great (33 and 75 mm.) with very high, identical pressures in the right ventricle; conversely, the differences in pressure varied widely (20 mm. and 50 mm., respectively) with the same diameter of the pulmonary artery (71 and 73 mm.).

In the patients with idiopathic dilatation of the pulmonary artery, widenings have been found of the same nature as in cases of pulmonary stenosis (fig. 8). In all patients with idiopathic dilatation, a systolic murmur was

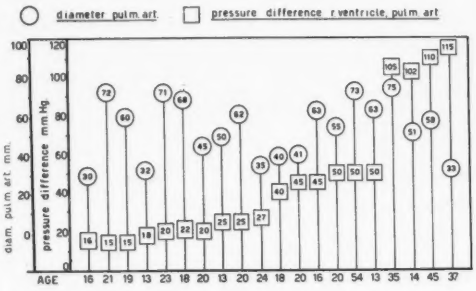


FIG. 4. Diagrammatic presentation of data.

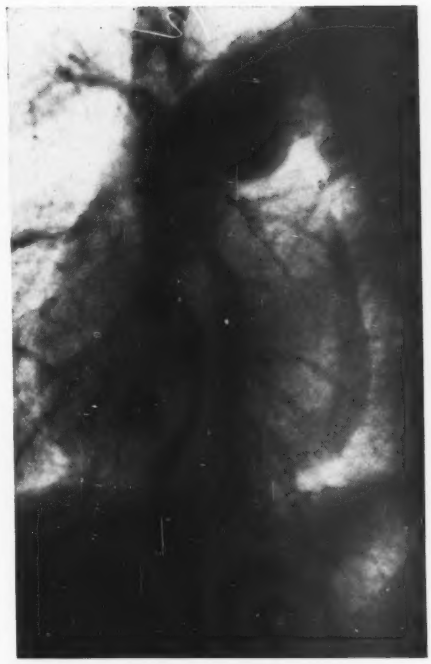


FIG. 6. Ha., age 20. Angiocardiogram made at 3.5 seconds. Pressure right ventricle, 60/0; pulmonary artery 15/8; diameter of pulmonary artery, 41 mm.

FIG. 5. R. L., age 21. Angiocardiogram made at 3.5 seconds. Pressure right ventricle 35/0; pulmonary artery 20/10. diameter of pulmonary artery, 73 mm.

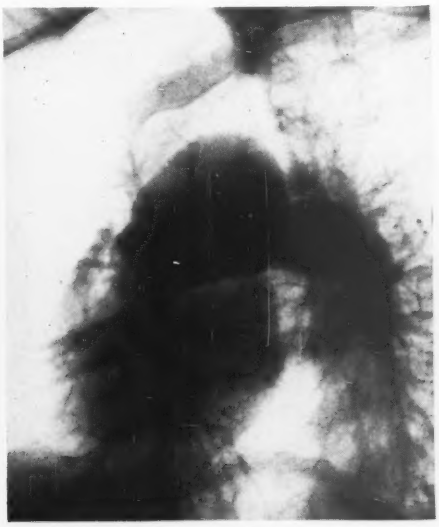
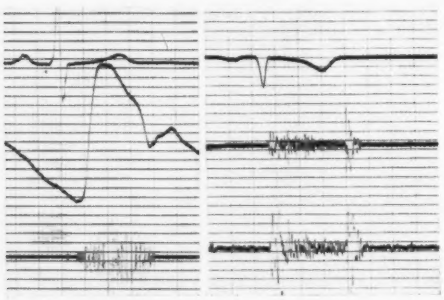


FIG. 7. I. B., age 16. Angiocardiogram made at four seconds; pressure right ventricle, 60/0; pulmonary artery, 15/2. Diameter of pulmonary artery, 63 mm.

audible in the second left intercostal space; the phonocardiographic form of the murmur was not the typical "diamond shape" as in pulmonary stenosis (fig. 9*A* and *B*). Just as was the case in the patients with pure pulmonary stenosis, there were no significant differences in oxygen saturation in superior vena cava, right atrium, right ventricle and pulmonary artery, and the arterial oxygen saturation was normal.

FIG. 8. G. H., age 15, angiocardiogram made at two seconds. Idiopathic dilatation of the pulmonary artery. Pressure right ventricle, 25/0; pulmonary artery, 20/5. Diameter of pulmonary artery 49 mm.



A *B*

FIG. 9*A*. Phonocardiogram in a case of pulmonary stenosis. *B* Phonocardiogram in a case of idiopathic dilatation of pulmonary artery.

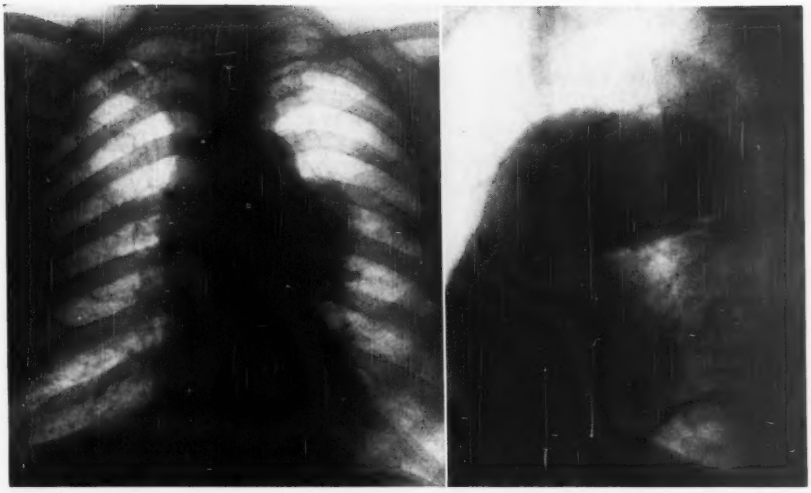
TABLE 1.—*Diameter Pulmonary Artery and Pressures Right Ventricle and Pulmonary Artery in Cases in Pure Pulmonary Stenosis*

NAME	AGE	DIAM. PULM.ART.	PRESSURE (mmHg) R.VENTR.	PULM. ART.	E.C.G.
P. S.	16	30 mm	34/2	18/6	normal
R. L.	21	72 mm	35/0	20/10	normal
G. D.	19	60 mm	35/5	20/7	normal
v.d. B.	13	32 mm	35/5	17/10	normal
H. H.	23	71 mm	40/0	20/5	r. bundle br. blok
H. S.	18	68 mm	42/2	20/6	normal
Sd.V.	20	45 mm	45/0	25/8	normal
L. B.	13	50 mm	45/0	20/5	r. bundle br. blok
R. B.	20	62 mm	45/0	20/10	r. bundle br. blok
A. X.	24	35 mm	55/0	28/12	incompl. r.b.br. blok
M.	18	40 mm	60/3	20/5	normal
Ha.	20	41 mm	60/0	15/8	normal
J. B.	16	63 mm	60/0	15/2	normal
Sn.	20	55 mm	70/0	20/5	normal
P. B.	54	73 mm	70/0	20/5	normal
Ho.	13	63 mm	75/0	25/10	r. bundle br. blok
A.W.	35	75 mm	120/0	15/5	incompl. r.b.br. blok
Gr.	14	51 mm	125/0	23/10	right ventr. strain
Ge.	45	58 mm	130/0	20/7	right ventr. strain
We.	37	33 mm	130/0	15/5	right ventr. hypertr.

TABLE 2.—*Diameter Pulmonary Artery and Pressures Right Ventricle and Pulmonary Artery in Cases of Idiopathic Dilatation of the Pulmonary Artery*

NAME	AGE	DIAM. PULM.ART.	PRESSURE (mmHg) R.VENTR.	PULM.ART.	E.C.G.
F.D.	15	42 mm	28/0	27/12	normal
H.H.	19	46 mm	25/0	25/0	normal
S.D.	25	49 mm	28/0	28/5	normal
G.H.	15	49 mm	25/0	20/5	normal
K.K.	20	40 mm	20/0	18/10	normal
R.G.	14	39 mm	25/10	25/10	normal

Here we wish to mention patient P. B., a 54 year old woman, who also had a moderate pulmonary stenosis (pressure in right ventricle 70/0 mm. Hg, in pulmonary artery 20/5 mm. Hg) with very severe dilatation of the pulmonary artery (73 mm.) suggestive of a mediastinal tumor (fig. 10*A* and *B*); so large in fact that it may be called an aneurysm. She was completely symptom-free and had gone



A *B*

FIG. 10. *A*, P. B., age 54, pulmonary stenosis and aneurysm of the pulmonary artery. *B*, angiocardiogram made at 3.5 seconds. Pressure right ventricle, 70/0; pulmonary artery, 20/5, diameter of pulmonary artery, 73 mm.

through seven pregnancies without any trouble. The electrocardiogram was normal.

DISCUSSION

The above observations show that there is no correlation at all between the dilatation of the pulmonary artery and the pressure in the right ventricle, and the difference in pressure between right ventricle and pulmonary artery (fig. 4). Dow and co-workers[4] also found that "the degree of enlargement of the pulmonary trunk appeared to bear no relationship to the degree of stenosis".

The dilatation of the pulmonary artery may be completely absent both in mild and in severe cases of pulmonary stenosis. This agrees with the autopsy findings described by Greene and associates[5] who found no dilatation of the pulmonary artery in 19 of 68 autopsy cases of pulmonary stenosis.[3] Routier and Escalle[9] found a dilated pulmonary artery in only 42 per cent of autopsied cases.

Widening of the same nature exists in the case of idiopathic dilatation of the pulmonary artery, although there is no stenosis of this artery.

These facts constitute arguments in favor of Laubry's[8] suggestion that we are dealing with two different congenital abnormalities, namely, valvular stenosis and dilatation of the pulmonary artery. The frequent concurrence of these two defects can be explained embryologically, because the development of the pulmonary valves and of the trunk of the pulmonary artery takes place in the same phase of embryological development.

Although there evidently exists a primary abnormality of the pulmonary artery, nevertheless the "hydraulic forces", described by Holman,[7] may certainly contribute to the final development of the dilatation.

CONCLUSIONS AND SUMMARY

In pure pulmonary stenosis, the diameter of the pulmonary arteries, as determined by means of angiocardiograms, proved to vary widely. There was no correlation of the size of the pulmonary artery with the pressure in the right ventricle and with the difference in pressure between right ventricle and pulmonary artery. The dilatation may be absent, both in mild and severe cases of stenosis. In idiopathic dilatation of the pulmonary artery, indis-

tinguishable widening of the same nature exists without pulmonary stenosis.

On the strength of these observations it is concluded that two different congenital defects should be recognized, namely, an abnormality of the pulmonary artery and valvular stenosis.

Summario in Interlingua

In pur stenosis pulmonar, le diametro del arterias pulmonar, determinate angiocardiographicamente, se provava grandemente variabile. Il habeva nulle correlation del largor del arterias pulmonar con le pressiones dexteroventricular o con le differentias pressional inter le ventriculo dextere e le arteria pulmonar. Dilatation pote esser absente tanto in leve como in sever casos de stenosis. In dilatation idiopathic del arteria pulmonar un allargamento del mesme natura existe sin stenosis pulmonar.

Super le base de iste observationes nos conclude que duo differente defectos congenite deberea esser recognoscite, i.e. un anormalitate del arteria pulmonar e stenosis valvular.

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Current Indications for the Use of Anticoagulant Drugs in Cerebrovascular Disease

By Robert G. Siekert, M.D., Clark H. Millikan, M.D., and Richard M. Shick, M.D.

Considerable variation exists in the interplay of the factors influencing the occurrence of strokes and their final outcome. A final statement about the usefulness of anticoagulant drugs in the treatment of cerebrovascular disease must await further study. The current indications for their use include: (1) intermittent insufficiency of the basilar arterial system, (2) intermittent insufficiency of the internal carotid system, (3) thrombosis within the basilar arterial system, (4) recurrent cerebral emboli associated with a likely cardiac source and (5) possibly, recurrent cerebral thromboses.

PHYSICIANS concerned with diseases of the vascular system in general are well acquainted with the commonness of cerebrovascular disease, the problems it presents, and the therapeutic difficulties involved. General care and rehabilitation of patients with strokes have been greatly expanded in recent years, and these contributions cannot be minimized. Yet, satisfactory treatment also implies prevention and, in the present context, avoidance of cerebral damage. Thus, we have been concerned with the concepts of early diagnosis and early treatment.

Anticoagulants as therapeutic drugs in cerebrovascular disease were suggested by Allen and Barker[1] more than 10 years ago. Although administered since then for recurrent cerebral emboli, anticoagulant drugs have been little used in the common variety of stroke. The lurking fears of intracerebral hemorrhage, and the causation of gross bleeding into an infarct by such treatment, have been the basis for much wariness. These fears are still present today and suggest caution in the use of anticoagulant therapy. This treatment is not to be recommended at this time as a "routine" for all strokes; it must be sharply limited to certain categories.

Originally it was recalled that a thrombus closing the basilar artery frequently had a laminated appearance. But of more importance were the facts that neurologic abnormalities often progress in steplike fashion when this artery becomes occluded and that transient episodes of neurologic dysfunction are common antecedent occurrences in such patients.[2] These observations suggested the usefulness of anticoagulant therapy in preventing the devastating and often fatal result of thrombosis of the basilar artery. Occlusive disease of the basilar arterial system appeared to have a course that might be interrupted by appropriate treatment. The concept of preventing any cerebral damage or more cerebral damage became apparent. In a similar way, episodic symptoms due to insufficiency of the carotid arterial system were looked on also as precursors of occlusion of the internal carotid artery.

Indications

The current indications for anticoagulant therapy in cerebrovascular disease are limited sharply to certain categories. They include the following: (1) the syndrome of intermittent insufficiency of the basilar arterial system, (2) the syndrome of intermittent insufficiency of the carotid arterial system, (3) thrombosis within the basilar arterial system, (4) recur-

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rent cerebral emboli, and (5) possibly, multiple strokes. Each of these categories is discussed separately.

The Syndrome of Intermittent Insufficiency of the Basilar Arterial System. This syndrome consists of transient episodes of neurologic abnormalities, such as weakness of the limbs, dimness of vision, diplopia, dysphagia, dysarthria, vertigo, numbness, and confusion, in various combinations.[3] When weakness on opposite sides of the body in separate attacks, poor vision, diplopia, vertigo, and pseudobulbar and bulbar phenomena are present, the diagnosis of intermittent insufficiency of the basilar arterial system would appear to be in order. Report of a typical case follows.

Case 1. A 64 year old man complained of "blind staggers" and "locking of the arms and legs." Save for a heart attack 15 months before his admission, he was well until 3 weeks prior to registration at the Mayo Clinic. At that time episodes began, characterized by decreased vision, unsteady gait, vertigo, and dysarthria. They lasted about 2 to 5 minutes and varied in severity. He averaged one of these spells per day. In addition, he had spells of hemiparesis, numbness, and paresthesia of the right or left limbs. With each spell, regardless of the side involved, he noted numbness of the lips and perioral region. He had had about a dozen attacks involving each side. He was free of any spell for only a few days during this 3-week period; often the attacks occurred up to 5 times a day. Rest in a hospital for a week and administration of aminophyllin and nicotinic acid were without apparent influence on the frequency of these spells.

The results of general and neurologic examinations were normal. He was normotensive. During an attack speech was weak and dysarthric (without evidence of aphasia), the left corner of the mouth drooped, and the tongue, pharynx, and palate moved poorly. Three minutes later the episode was over and examination did not show any abnormalities. Heparin, tromexan, and dicumarol were administered. He had one brief attack just prior to the fifth injection of heparin and none since.

The Syndrome of Intermittent Insufficiency of the Carotid Arterial System. This syndrome consists of transient episodes of unilateral impairment of motor or sensory function, or both, associated often with involvement of vision homolateral to the affected artery and a disorder of speech, frequently aphasia, if the dominant hemisphere is involved.[4] Decrease in the retinal arterial blood pressure and in the pulsation of the common or internal carotid artery may be present.

Case 2. A 77 year old man was seen in July 1955, because during the preceding 6 weeks he had episodes of poor use of the left hand. The first episode occurred while he was driving his car; he suddenly noted that his left hand felt heavy and useless. It was awkward, felt numb and he could barely move it. Within 20 minutes the spell disappeared and he felt normal. He had similar attacks daily that lasted from 20 to 30 minutes. The attacks became severer, so that the arm also was involved. However, he had not had headaches or difficulty with vision or speech in association with these episodes. On the day before admission, and on the day of admission to the clinic, he had 2 or 3 episodes. Recovery from the recent spells was not quite complete.

Examination disclosed slight hyperactivity of the left biceps jerk and a -1 to -2 decrease in alternate-motion rate of the left hand. The pulsations of the right carotid artery were slightly diminished. Ophthalmodynamometer reading for the right eye was 38 mm. of mercury and that for the left, 60 mm., consistent with an occlusive process in the right internal carotid artery. Roentgenograms of the skull showed no evidence of abnormality. An electroencephalogram showed minimal dysrhythmia in the right hemisphere. An electrocardiogram showed ventricular premature contractions and evidence of left bundle branch block. Anticoagulant therapy was begun with dicumarol and tromexan. After effective anticoagulant action was obtained, he had no further spells.

Comment. Anticoagulant drugs have been administered to 33 patients with the two syndromes of insufficiency mentioned above; in 22 the basilar system was implicated and in 11 the internal carotid artery was involved. The attacks promptly abated after effective anticoagulant levels were obtained, and it is believed that these drugs are a prime factor in stopping these episodes.[5, 6] Since the periodic attacks often precede thrombosis of the main arteries and progression appears to be thwarted by anticoagulant drugs, one might infer that cerebral damage has been prevented.

It is too early to compare a "control" series, for the length of time patients have suffered from these episodes has varied a great deal. Some patients have had such spells for several years without apparent progression in their

disease and others have died after only a few attacks.

It is only too obvious that these two syndromes could encompass all episodes of cerebrovascular insufficiency. Among other things, however, careful delineation of the condition is an important means of avoiding pitfalls in diagnosis and, since our knowledge is incomplete, of limiting the use of these drugs to well-defined syndromes.

Thrombosis within the Basilar Arterial System. About two thirds of the patients who sustain occlusion of the basilar artery itself have histories of antecedent episodes of insufficiency to this system.[2] When permanent damage has occurred, examination must indicate the lesion to be in the region supplied by the basilar arterial system. Neurologic abnormalities will include hemiparesis or quadriparesis, dysarthria, dysphagia, oculorotatory and pupillary abnormalities, superficial sensory loss, often bilateral or crossed face and body, and bilateral homonymous field defects. These neurologic abnormalities tend to advance and interruption of their progression is the goal of treatment.

Case 3. A 72 year old man registered at the clinic and was admitted to the hospital on August 8, 1955, because of difficulty in speaking and weakness of the left limbs.

During the preceding 2 months he had a number of episodes of dragging of the right foot, drooping of the right corner of the mouth, and slurred speech. Additionally, he had a number of attacks of dizziness and on one occasion, after a severe spell, he was somnolent for 6 hours. He was known to have been hypertensive for 10 years.

Early on the day of admission he suddenly fell and was "stiff" for a brief period. His blood pressure was said to have been 210 mm. of mercury systolic and 150 mm. diastolic and he was noted to be anarthric. Throughout that day he had periods during which he could talk well; at other times he had slurred speech or anarthria.

Examination some 12 hours after the ictus disclosed a blood pressure of 140 mm. systolic and 90 mm. diastolic, right-sided Horner's syndrome, left lower facial palsy, dysarthria, labored swallowing, weak palatal elevation, weakness of the left side of the tongue, left hemiparesis with ankle clonus, and Babinski's sign. During the examination it was noted that his condition fluctuated, at times being hemiplegic, although he never became normal. On several occasions Chaddock's sign was noted on the right side. The administration of heparin, dicumarol, and tromexan was begun immediately. His condition stabilized and his abnormalities lessened. At the time of his dismissal 2 weeks later, he had only minimal slowness in alternate-motion rate of the left limbs and slightly hyperactive reflexes on the left.

Comment. About 50 patients with this lesion have been treated to date with anticoagulant drugs. There have been a striking decrease in mortality (as compared with a contrast group) and surprising improvement in the neurologic abnormalities. Data on the original group showed that 14 per cent of patients receiving anticoagulant therapy died, while 43 per cent of a contrast group (not receiving such therapy) died.[3]

Recurrent Cerebral Emboli. These emboli may be associated with atrial fibrillation, rheumatic heart disease and myocardial infarction and they provide another indication for anticoagulant therapy. Wright and McDevitt[7] have clearly pointed out the tremendous value of anticoagulants in the preventive treatment of such phenomena.

Multiple Strokes. Some patients who appear subject to recurrent cerebral thromboses, presumably supratentorial and often bilateral, also may benefit from anticoagulant therapy in the sense of prevention. Since only a few patients have been treated in this indeterminate group, this condition is a questionable indication at this time.

Comment

In any discussion of strokes, it must be remembered that considerable variation exists in the interplay of the factors influencing their occurrence and their final outcome. Assessment of any therapy is extremely difficult. Further study must be applied to the treatment with anticoagulant drugs before a final statement can be made about their usefulness in the treatment of cerebrovascular disease. On the basis of present knowledge, however, this treatment appears to be of definite value in the first four conditions discussed.

Careful diagnosis of the particular type of cerebrovascular involvement is essential. This

applies particularly to those instances of episodic symptoms, where the examination reveals normal findings unless an attack is observed. There is no diagnostic test, although appropriate laboratory studies are important aids in excluding other likely disorders. A single survey is not enough. Continued assessment of each patient is needed, for other lesions may be mimicking cerebrovascular disease and the course of the illness will aid in their differentiation.

In each case the general contraindications to anticoagulant therapy, both absolute and relative, must be considered. Many are relative, for we have not hesitated to use anticoagulant therapy in the treatment of certain patients with histories of duodenal ulcer who have early and advancing thrombosis of the basilar artery. On the other hand, the outlook for a patient with occlusion of the posterior inferior cerebellar artery is, in general, good, so that anticoagulants would be withheld in the presence of such a contraindication.

In those instances in which rapid action is required, heparin has been employed early. Otherwise, tromexan and dicumarol have been used, the latter for long-term management. Usually we have suggested use of the anticoagulants for an indefinite period, but in two instances of intermittent basilar insufficiency they were discontinued after three months and the patients have not had a recurrence of the episodes. On the other hand, discontinuance of anticoagulants in patients with thrombosis of the basilar artery itself has been associated in several cases with rapid progression of the illness.

Since it appears that anticoagulant drugs eliminate the transitory episodes, some action they possess must be included in a consideration of the pathogenesis of these states of insufficiency, although it is probable that a number of factors are involved.[6]

Summary

The current indications for anticoagulant therapy in cerebrovascular disease include: (1) intermittent insufficiency of the basilar arterial system, (2) intermittent insufficiency of the internal carotid system, (3) thrombosis within the basilar arterial system, (4) recurrent cerebral emboli associated with a likely cardiac source and (5) possibly, recurrent cerebral thromboses.

Summario in Interlingua

Sub le conditiones currente, le indicationes pro le uso de drogas anticoagulante in le therapia de morbos cerebro-vascular include (1) intermittente insufficientia del systema de arteria basilar, (2) intermittente insufficientia del systema de carotide interne, (3) thrombosis intra le systema de arteria basilar, (4) recurrent embolos cerebral associate con un probabile origine cardiac, e (5) possibilemente, recurrente thromboses cerebral.

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Portable Serial Roentgenkymography in Acute Myocardial Infarction

By J. J. Sampson, M.D., L. R. Felton, M.D., A. A. Goetz, M.D., B. Solomon, M.D., and B. Axelrad, M.D.

Serial roentgenkymographic records were taken at the bedside of 31 patients with acute myocardial infarction. Most such tracings are adequate for determining "ballooning" (systolic reversal) and other defects of left ventricular contraction and expansion. These abnormalities are observed frequently in this condition and fluctuate from day to day, appearing or disappearing at various rates. Ballooning is the most serious defect, in that it was observed in the roentgenkymograms of all the patients who died and in all those with severe shock. Serial roentgenkymograms are of value as diagnostic aids, as evidence of the immediate and changing functional state of the myocardium and as an index of prognosis. They may herald further extension of the infarct or ventricular rupture. Roentgenkymographic abnormalities, including ballooning, may persist after clinical recovery.

CERTAIN abnormalities in ventricular movement, both in systole and diastole, have been observed during the course of myocardial infarction by fluoroscopic,[1] roentgenkymographic,[2-5] and electrokymographic means.[6-14] The systolic abnormalities consist of (a) delay in the onset or rate of normal systolic retraction of the ventricular wall, (b) marked diminution or absence of retraction waves, and (c) actual reversal of the usual retraction and the occurrence of expansion ("ballooning").[8-16] The diastolic abnormalities are seen usually only in those cases in which there is an abnormality of the systolic contraction curve. They consist either of no expansion of the ventricular wall or of paradoxical retraction for part or all of the diastolic period.[1, 8, 9, 12, 13, 18]

These abnormalities, although they may occur in various other types of cardiac disorders,[16-21] are most often associated with myocardial infarction. This is because diminution or reversal of retraction of the ventricular wall in systole occurs most often in a myocardium weakened by necrosis or ischemia, or both.[22-24] The seriousness of systolic reversal is shown by the fact that if sufficiently severe and extensive, it can lead to failure of cardiac output and, possibly, to death. It may, however, be present without signs or symptoms of heart failure.

Although these characteristic patterns have been observed frequently in myocardial infarction, we know of no studies based on frequent *serial* roentgenkymographic records and their correlation with the clinical status of the patients. The purpose of this paper is to report on 31 patients suffering from acute myocardial infarction who were studied by means of bedside roentgenkymograms taken during the first 72 hours of their illness and subsequently every 24 to 48 hours for 5 to 10 days and less frequently until their death or hospital discharge. The data obtained were classified to determine if the abnormalities observed by roentgenkymographic means could be correlated with the clinical status of the patients and if they carried any diagnostic and, especially, any prognostic significance.

Materials and Methods

The study consisted of 31 patients with electrocardiographic and clinical evidence of myocardial infarction. Twenty-three were males and 8 females; their ages ranged from 43 to 87 years. The location of the infarct as established by electrocardiograms was as follows: anteroseptal, 10 cases; anterolateral, 9 cases; posterolateral, 4 cases; posterior, 8 cases. Nine of the patients had had previous myocardial infarcts; 22 had not.

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The cases were classified as to degree of clinical severity as follows:

"Mild." No evidence of shock or heart failure and no serious complications, 6 cases.

"Mild failure." Transient pulmonary basal rales, 7 cases.

"Moderate to severe." Persistent rales and other evidence of serious involvement (recurrent severe pain, oliguria, nausea and vomiting, transient blood pressure levels below 90 mm. Hg systolic, tachycardia of greater than 110 beats per minute, rectal temperature elevation over 38 C., and persistent arrhythmias), 8 cases.

"Shock." Hypotension for at least 45 minutes with systolic blood pressure below 90 mm. Hg, 10 cases.

Roentgenkymographic tracings were taken within 24 hours of the onset of myocardial infarction in 21 cases and within 72 hours in the remaining 10. Successive records were made daily for 4 or 5 days in 25 cases and on at least alternate days in the remaining 6. In 27 instances additional films were taken every 3 to 7 days until death (4 patients) or discharge.

Roentgenkymographs* were taken in the anteroposterior projection, except in a few instances when left anterior oblique exposures were made. Dack and associates[11, 12] and others, have found that anteroposterior exposures reveal abnormal contractions with great consistency, regardless of the site of the lesion in the left ventricle. The tracings were made with the patient in a semierect sitting position in bed, leaning back against the smooth surface of the roentgenkymograph. The roentgen tube, supported by a bracket on a horizontal rod attached to a mobile vertical standard, was placed anteriorly to the patient's chest. In general, bedside roentgenkymography produces no untoward emotional reactions in the patient. The procedure is contraindicated, however, in certain patients in severe shock who cannot be maintained in the semierect position without further fall of blood pressure.

The roentgenkymographic tracings were studied by photographing the x-ray film on a standard 8.3 by 10.2 cm. lantern slide, and then projecting the photograph on a screen 15 to 20 feet distant. The projections were enlarged three- or fourfold to produce complete cardiac cycles of 3 cm. in length. The representative tracings (fig. 4, 6 and 7) were made from such enlargements. Minor deviations in these tracings were disregarded and only major directional patterns were recognized in the interpretations.

For simplicity of presentation, roentgenkymographic abnormalities of the left heart border were grouped in arbitrary order of descending severity as: *type 1*, "systolic reversal," i.e., expansion (or ballooning) of the major portion of the systolic period; *type 2*, "systolic and diastolic abnormalities," i.e., delayed initial systolic contraction or late systolic expansion, or partial diastolic collapse or mesial motion of the border during some portion of diastole; and *type 3*, "flattened," i.e., a flattened pattern and poorly defined waves in systole and diastole. Calculation of the percentage of abnormalities was based on the occurrence sometime during the course of illness of the three types of roentgenkymographic abnormalities. If two or more abnormal forms were observed in the same patient's records, however, only the "dominant" or presumptively most significant defect was entered in the figures.

These abnormalities were also grouped by location as high ventricular, midventricular and low ventricular or apical.

Results

Roentgenkymographic abnormalities of the left cardiac border (fig. 1) were observed in 24 (77 per cent) of the 31 cases at some time during the course of acute myocardial infarction. Systolic reversal, with or without other abnormalities, was noted in 16 (52 per cent) of the patients; other systolic and diastolic abnormalities, but not complete systolic reversal or flattening, in 11 (35 per cent); and flattening, with or without other deviations, with the exception of major systolic reversal (ballooning), in 7 (23 per cent). In the majority of the cases these changes appeared early in the course of infarction; 70 per cent of the patients examined within the first 24 hours after an attack showed some roentgenkymographic deviation.

Of the 27 patients who survived, 13 (48 per cent) had normal roentgenkymograms at the time of discharge from the hospital (fig. 1). The records of six of these patients had shown abnormalities previously; in the remaining seven, the roentgenkymograms had been normal at all times. In 14 cases (52 per cent) the

* The apparatus used was a Liebel-Flarsheim model K3 multiple slit kymograph with slits at 12 mm. distance and the film moving at determined rates behind the slits. The portable generator (Picker Co.) delivered from 30 ma. at 100 v to 60 ma. at 220 v. The distance from the tube target to the skin varied from 63 cm. to 76 cm., and to the film approximately 110 cm. The output was from 30 to 60 ma./sec. at 80 to 90 kv. A 1 mm. aluminum filter was used. This dosage of radiation is considered free of hazard to the patient for as many as 20 records taken within three weeks.

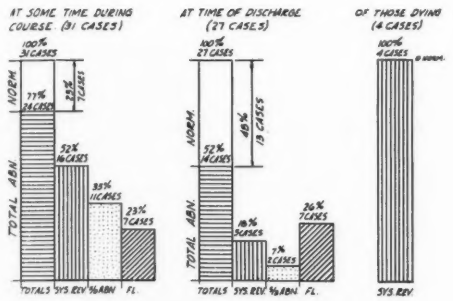

FIG. 1. Frequency of occurrence of roentgenkymographic abnormalities in myocardial infarction. The first set of columns indicates the appearance of an abnormality alone, or in combination with other abnormalities, at some time during the course of illness in the 31 patients studied. Abnormalities are listed as *Sys. Rev.*, extensive systolic expansion or ballooning, *S/D Abn.*, other types of abnormal forms in the systolic or diastolic curves, and *Fl.*, flattening of the entire pattern. The cases total more than 100 per cent, since different abnormalities may appear in the same patient at different times.

final records still showed deviations: local ballooning in 5 (18 per cent), flattening in 7 (26 per cent) and other abnormalities in 2 (7 per cent). In no case was there fluoroscopic or roentgenographic evidence of massive paradoxic motion or local distention of the ventricle suggesting ventricular aneurysm.

The 5 patients whose final records showed localized systolic reversal (fig. 1) had no cardiac enlargement or evidence of heart failure at the time of discharge, although other observers[8, 9, 11, 14, 22] have noted their occurrence several months after clinical recovery from attack in patients with apparently normal cardiac function. The followup of the surviving patients in our group, however, was not long enough to determine the eventual course in such cases.

It is possible that local ballooning may have been present at the onset of the current attack in those patients with histories of previous infarction. Ballooning was noted in the first roentgenkymograms in 7 of the 9 patients with such histories, but in only 6 of the 22 who had no known previous attack. It is apparent that defects of myocardial contractions, especially systolic reversal, are more prevalent and that mortality is higher after successive attacks.

The frequency of the three types of abnormalities according to the position of the heart border and the presumptive site of the infarct as determined by electrocardiogram is shown in figure 2. The high percentage of normal curves in the group with anteroseptal infarcts suggests that lesions in the mesial position do not affect a large enough area of the myocardium to alter the left heart border. However, when the lesion is so extensive that its effect extends to the left border of the heart, ballooning of a wide area occurs. Also, less distinctive forms of abnormal tracings than ballooning are produced when the myocardium is less seriously impaired. Posterolateral infarcts (inferior surface), as might be expected, involve the apex uniformly and thus may alter myocardial function at both high and low levels, depending on their location.

A close relationship exists between the clinical status of the patient and the incidence and frequency of roentgenkymographic abnormalities. In our patients the incidence of all abnormalities, particularly systolic reversal, was proportionate to the clinical evidence of the severity of the infarct. Systolic reversal was not observed in patients who had "mild" attacks, but was noted in each of the four patients who died (fig. 1).

Experiments on animals have shown that the duration of dominant abnormalities of

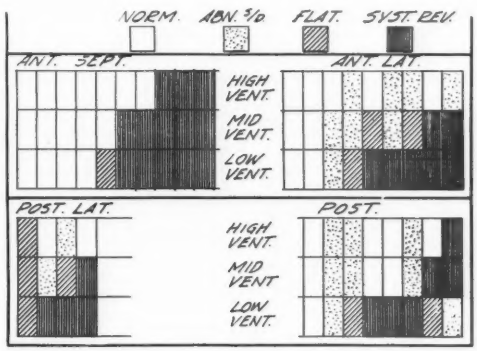

FIG. 2. Location of infarcts in relation to location of roentgenkymographic abnormalities.

contraction in the areas surrounding a myocardial infarction varies according to the degree and duration of hypoxia and the load of work of the heart.[22] In 17 of our 31 cases adequate roentgenkymograms were obtained on the first day and with sufficient frequency thereafter to show (1) the rate of change from normal patterns or minor abnormalities to systolic reversal, (2) the recession of a systolic reversal to a lesser abnormality and (3) the recovery from all abnormalities and return to a normal pattern.

Systolic reversal appeared abruptly within one day in 4 patients, 3 of whom died; in a fifth case it appeared slowly. In six patients, all of whom recovered, the ballooning disappeared, either rapidly or slowly; apparently the muscle had partially or completely regained contractile function at the time of discharge from the hospital. In a third group of six patients who exhibited no abnormalities at the time of discharge, the complete recession of abnormalities took place slowly.

Illustrative Case Histories

The following case histories serve to illustrate certain features, namely:

1. The diagnostic value of records taken shortly after the onset of an attack.
2. The heralding, by changing patterns of the records on the preceding day, of the clinical and electrocardiographic evidence of an extension of the infarction.
3. The transient appearance of "ballooning" accompanying mild shock.
4. The heralding of ventricular rupture by a broadening of the area of abnormal contraction without the warning of clinical signs or symptoms.
5. The effect of elevation of blood pressure by L-norepinephrine on the pattern of myocardial contraction.

For purposes of comparison, the roentgenkymographic tracings in a normal man, aged 35, and the tracing of enlarged frames are shown in figures 3 and 4. The onset of systole as timed from the onset of aortic expansion is indicated by horizontal lines.

In two cases, the records of which are not

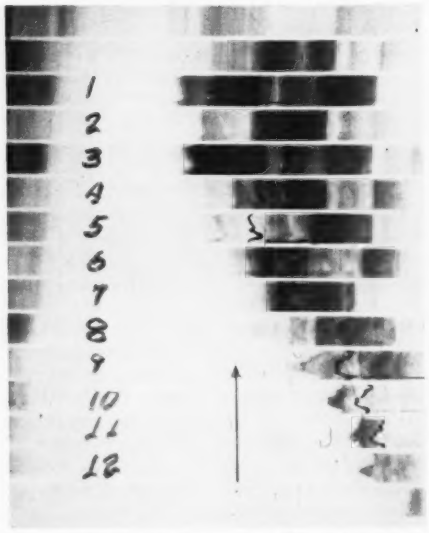

Fig. 3. Roentgenkymogram of normal male, aged 35 years.

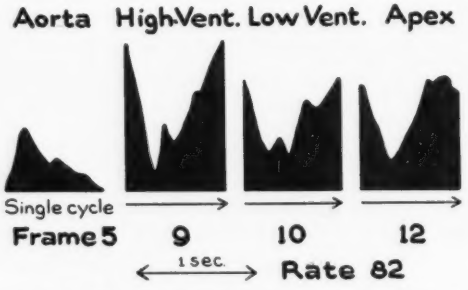

Fig. 4. Tracing of enlarged projection of certain frames of figure 3.

presented here, the patients had persistent precordial pain for two and five hours, respectively, before the attack of acute myocardial infarction, but no electrocardiographic evidence of infarction for 36 and 70 hours, respectively. Systolic reversal was noted in each patient within 24 hours of the onset of pain; this finding pointed toward the diagnosis of an infarct.

Case 1. W. L., male, aged 48 years, with no previous history of heart disease, had a characteristic attack of precordial compressing pain on the first day of his illness and electrocardiographic evidence of a posterolateral infarction on the second day. A

roentgenkymogram taken on the second day, 20 hours after the onset of pain, showed flattening of the apical contraction. Another roentgenkymogram taken on the eleventh day revealed ballooning (fig. 5). Figure 6 is an assembly of the enlarged tracing of one cardiac cycle starting with the aortic-timed onset of systole on the second, third, fifth, seventh and fourteenth days.

On the seventh day the patient was more pallid and sweated heavily; his blood pressure fell slightly. On this day, early systole exhibited an expansile form (fig. 6, frame 10). On the eighth day a recurrence of severe persistent pain necessitated a subcutaneous dose of 100 mg. of Demerol, which relieved

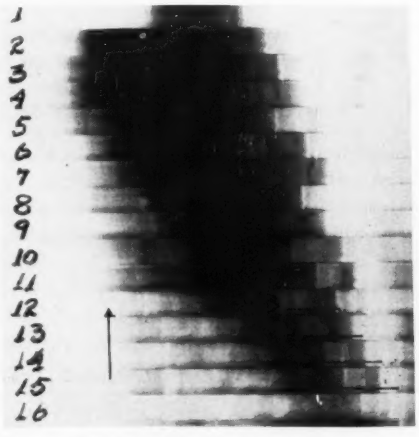

FIG. 5. Roentgenkymogram of W. L., male, aged 48 years. Myocardial infarction, eleventh day of illness.

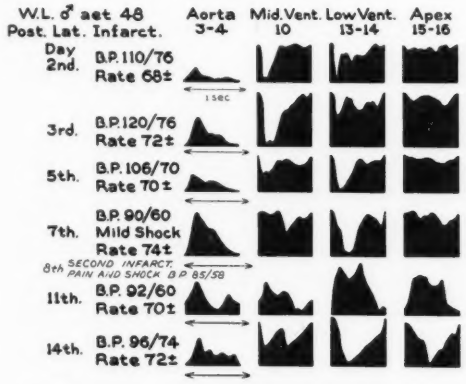

FIG. 6. Tracings of roentgenkymograms of patient W. L., male, aged 48, on several days of illness. The numerals on line 2 refer to frame numbers of the roentgenkymogram.

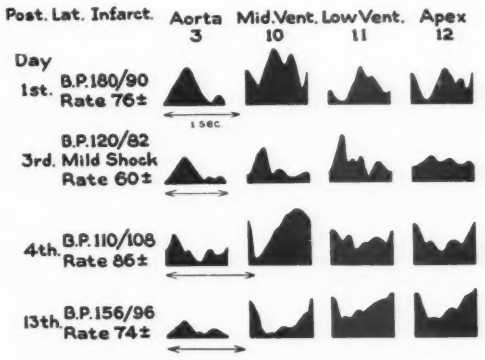

FIG. 7. Tracings of roentgenkymograms of J. P., male, aged 41, on several days after onset of myocardial infarction. The numerals on line 3 refer to the frame numbers of the roentgenkymogram.

the pain in 2 hours. On the ninth day the patient's temperature rose, and an electrocardiogram indicated an extension of the infarction further anteriorly (inversions of T waves in leads V 5–6). Roentgenkymograms taken on the ninth and eleventh days showed systolic expansion in the mid and lower ventricle (fig. 5, frames 12–15, and fig. 6, frames 10–16), as timed with aortic expansion (fig. 6, frames 4 and 5). By the fourteenth day systolic contraction had returned (fig. 6), but was irregular (frame 10) and delayed (frames 15 and 16). The patient made an uneventful recovery and was discharged from the hospital on the twenty-eighth day.

This case illustrates that modification of myocardial contraction is probably associated with diminishing local coronary blood supply and that it may be accompanied by indefinite clinical signs that precede the characteristic onset of a secondary infarct as indicated by prolonged pain and electrocardiographic changes.

Case 2. J. P., male, aged 41, who had hypertension for the previous 7 years and angina pectoris for 16 months, developed severe, persistent substernal pain lasting 6 hours, which was partially controlled by subcutaneous injections of morphine. An electrocardiogram revealed a pattern characteristic of posterolateral infarct. Enlarged tracings from roentgenkymograms taken on the first, third, fourth and thirteenth days are shown in figure 7. On the first day the only definite abnormality was a shortened systolic contraction (frame 10). On the third day when mild shock appeared, ballooning was evidenced (frames 10 and 11) and flattening at the apex (frame 12). Twenty-four hours later (fourth day) early systolic contraction had returned in the midventricle, but flattening persisted in the low ventricle. By the thirteenth day systolic contraction,

although imperfect, was evident throughout the left cardiac border. The patient made an uneventful recovery and was discharged, ambulatory, on the twenty-fourth day.

This case illustrates the transiency of ballooning in local areas during mild shock and probable dependence on the adequacy of coronary blood supply and myocardial oxygenation.

Case 3. S. G., female, aged 70, who had shown no previous signs or symptoms of cardiac disorder, developed severe substernal pain radiating to the throat and back, which subsided in 4 hours without medication. During the next three days she had two or three episodes of spontaneous pain, lasting from 5 to 20 minutes. An electrocardiogram taken at this time revealed a high anterolateral infarct. A roentgenkymogram showed ballooning of the upper left ventricle on the first and fourth days and systolic reversal of the lower ventricular wall on the fourth day. At that time the patient felt quite well and appeared free of shock or heart failure. On the fifth day she died abruptly; an autopsy revealed rupture of the high posterolateral wall of the left ventricle.

This case illustrates the localization of a high left ventricular lesion and the possible prognostic significance of a widening of the area of systolic expansion in a patient who exhibited no other signs of impending ventricular rupture.

Case 4. M. H., male, aged 70, had angina pectoris for two and one-half years prior to the onset of severe left precordial pain radiating to the left arm. Three intramuscular doses of 100 mg. of Demerol within 4 hours were required to control the pain. An electrocardiogram was consistent with posterior myocardial infarction. Roentgenkymograms showed marked flattening of the waves at the apex from the first day to the morning of the fourth day. On the fourth day the patient's blood pressure fell abruptly from 106/72 to 72/40 mm. Hg, and he appeared to be in shock. L-norepinephrine, in a concentration of 8 mg./L. of 5 per cent glucose solution, was administered by intravenous drip infusion for 18 hours. The blood pressure rose promptly and was maintained by this therapy at levels over 100/64 mm. Hg. A roentgenkymogram taken one hour after the start of this therapy showed large, deep systolic contractions through the entire ventricular wall. A tracing taken on the eighth day showed a delayed systolic contraction high in the left ventricle, but the apical region maintained systolic contraction. In later records the patterns were approximately normal. The patient made an uneventful recovery.

This case illustrates the improvement of ventricular contraction that accompanies elevation of blood pressure and therefore more effective coronary arterial circulation. In addition, this change reflects the direct action of L-norepinephrine on myocardial contraction.

A similar case of myocardial infarction with severe shock was treated with L-norepinephrine. Continuous drip infusion maintained the blood pressure at satisfactory levels for 10 hours, at which time the patient abruptly died. The roentgenkymograms in this case showed increased amplitude of aortic expansion, but apical and midventricular flattening of curves was not modified. This suggests that inability of the myocardium to recover contractile quality despite adequate maintenance of blood pressure indicates a poor prognosis.

Summary and Conclusions

1. Roentgenkymographic tracings were made at the bedside of 31 patients with myocardial infarction. Although interpretation is sometimes difficult, such records are usually adequate for determining ballooning (systolic reversal) and other defects of left ventricular contraction and expansion.

2. Roentgenkymographic abnormalities were manifested by 77 per cent of the patients at some time during the course of the illness. Extensive ballooning during the systolic period was observed in 52 per cent, systolic and diastolic abnormalities in 35 per cent and flattening of the systolic and diastolic excursions in 23 per cent.

3. Defective ventricular contraction curves are sufficiently common during the early stages of attacks to serve as a diagnostic sign, but the absence of such an abnormality in a roentgenkymogram does not exclude myocardial infarction. Seventy per cent of the patients in our series exhibited roentgenkymographic abnormalities during the first 24 hours of the attack.

4. In man, as has been observed in experimental animals, the changes in the contraction patterns may occur abruptly and fluctuate from day to day, frequently without accompanying clinical or electrocardiographic manifestations.

5. In our series impaired contraction seemed

o herald the advancing ischemia prior to a econdary infarction in one case and to rupture f the ventricle in another.

6. Presumptive improvement of coronary irculation by relieving severe hypotension vith L-norepinephrine resulted in improved ontraction in one patient who recovered, but ad no observable effect in a second patient vho subsequently died.

7. Although there is no absolute correlation etween circulatory failure and ballooning, a igh incidence of ballooning was found in the oentgenkymograms of patients with shock and ther evidence of a severe attack.

8. Ballooning may occur without shock, but one of the patients who died and none with shock failed to exhibit this defect.

9. Previous infarction increased the tendency toward ballooning.

10. The roentgenkymograms of 18 per cent of the patients discharged as clinically free of signs of circulatory failure exhibited ballooning and 50 per cent showed some type of roentgenkymographic abnormality. One may assume that hypoxia or physical stress would be a hazard to patients manifesting this evidence of myocardial dysfunction.

Acknowledgment

The authors acknowledge, with thanks, the cooperation of the many physicians who permitted us to examine their patients for this study. We are also indebted to Mr. Raphael Sampson for the preparation of the charts and diagrams.

Summario in Interlingua

1. Registrationes roentgenokymographic esseva obtenite al lecto del patientes in 31 casos le infarcimento myocardial. Ben que le interpretation es a vices difficile, usualmente tal egistrationes es adequate pro determinar allonamento (reversion systolic) e altere deectos del contraction e expansion sinistroentricular.

2. Anormalitates roentgenokymographic esva manifestate per 77 pro cento del patientes un o altere tempore in le curso del maladia. n ballonamento extense durante le periodo ystolic esseva observate in 52 pro cento del casos, anormalitates systolic e diastolic in 35 pro cento, e applattamento del excursiones systolic e diastolic in 23 pro cento.

3. Defective curvas de contraction ventricular es sufficientemente commun durante le prime phases del attaccos pro servir como signos diagnostic, sed le absentia de un tal anormalitate ab le roentgenokymogramma non exclude le possibilitate de infarcimento myocardial. Septanta pro cento del patientes in nostre serie exhibiva anormalitates roentgenokymographic durante le prime 24 horas del attacco.

4. De accordo con observationes in animales experimental, le alterationes del figuration contractional in humanos pote occurrer abruptemente. Illo pote fluctuar ab un die al altere, frequentemente sin accompaniamento de manifestationes clinic e electrocardiographic.

5. In nostre serie, defectivitate del contraction pareva annunciar le progresso de ischemia ante le formation de un infarcimento in un caso e ante le ruptura del ventriculo in un altere.

6. Le melioration (presumptive) del circulation coronari effectuate per le uso de L-norepinephrina in le alleviation de sever hypotension resultava in contraction meliorate in un patiente qui recuperava, sed illo habeva nulle effecto observabile in un altere patiente qui moriva subsequentemente.

7. Ben que il non existe un absolute correlation inter disfallimento circulatori e ballonamento, un alte frequentia de ballonamento esseva trovate in le roentgenokymogrammas de patientes con choc e altere signos de un attacco sever.

8. Ballonamento pote occurrer sin choc, sed omne le patientes con choc e omnes qui moriva habeva ballonamento.

9. Previe infarcimentos augmentava le tendentia al ballonamento.

10. Le roentgenokymogrammas de 18 pro cento del patientes dimittite como clinicamente libere de signos de disfallimento circulatori exhibiva le phenomeno del ballonamento, e 50 cento monstrava le un o le altere typo de anormalitate roentgenokymographic. Il es a

supponer que hypoxia o stress physic esserea un hasardo pro patientes qui manifesta iste signo de dysfunction myocardial.

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An Accurate, Clinically Practical System For Spatial Vectorcardiography

By ERNEST FRANK, PH. D.

This paper describes a new improved system of spatial vectorcardiography that is practical for clinical use. It represents an optimum compromise among such factors as soundness of theoretic basis, accuracy, reproducibility, signal-to-noise ratio, and speed of application. Some of its advantages over currently employed systems include a rational physical basis, corrections for torso shape, avoidance of left arm, insensitivity to individual variability of ventricle location, and accuracy comparable to applicability of 3-dimensional torso-model data to the human subject. Detailed description of electrode placement, practical procedures, and useful technics is included.

AN accurate method for determining three orthogonal components of the human equivalent heart dipole has been the objective of an international search for many years. A clinically practical answer to this problem is presented here and represents the product of five years of intensive theoretic and experimental investigations.

All systems of spatial vectorcardiography now in general use suffer from a variety of substantial quantitative defects that are described conveniently in terms of image vectors associated with each lead. Image vectors (sometimes called lead vectors) are related to the equivalent heart dipole in such a manner that the projection of the heart dipole onto the image vector times its length yields potential difference of the lead.[1, 2] An ideal system of vectorcardiography would have 3 equal-length, orthogonal image vectors for all subjects. Experiments with accurate 3-dimensional homogeneous torso models, which apply with surprising accuracy to the human subject,[3-5] reveal that image vectors utilized in most systems[6-8] are not parallel to anatomic body axes, are not mutually perpendicular, are unequal in length (and improperly corrected by standardization factors employed), and, most seriously, are susceptible to variations traceable to change in anatomic location of the equivalent dipole from one subject to another.[9] Standard limb and precordial leads of clinical electrocardiography have similar defects,[10] but have been found useful nevertheless on an empiric basis for diagnosis of many heart disorders. Vectorcardiography appears to have resulted in little new information[11] despite its emphasis on relative timing of various leads. This is not too surprising in view of the errors mentioned above, and especially since limb and precordial leads, which have been studied exhaustively for many years, give the essence of most of the qualitative information available on the body surface. Moreover, vectorcardiography has not been fully exploited because projections of vector loops onto anatomic body axes have been commonly used rather than studying loops in their own frame of reference.

Further strides in electrocardiography are most likely to be made in the quantitative area. Before quantitative analysis may be made meaningful, however, it is essential to correct for many known errors in present methods, especially those arising from torso shape and individual variability in dipole location, left arm characteristics and anatomic orientation of the heart. The system of vectorcardiography proposed here has the express purpose of enabling quantitative studies by suitable correction of these known errors. It will produce vectorcardiograms of far greater accuracy than any system in current use.

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Whether or not this improved accuracy will enhance clinical diagnosis of heart disease remains to be demonstrated.

This system of vectorcardiography represents an optimum compromise among many conflicting factors, such as soundness of theoretic basis, accuracy, vulnerability to dipole location, ease and speed of application, reproducibility, signal-to-noise ratio, and cost. Its advantages over currently used methods are believed to outweigh by far its disadvantages.

General Description

Four electrodes are the minimum number required theoretically in any system of vectorcardiography, since three independent potential differences are necessary to determine the heart vector in three dimensions.[2, 6] From the standpoint of ease and speed of application and reproducibility, the 3 standard limb positions (right and left arms, left leg) and the back are superior sites. Torso-model data have been applied to these electrode sites as used in the modified Wilson tetrahedron,[6] and to an "average computing" type system[9] that incorporates torso-model corrections for an average ventricle center. Unfortunately major quantitative shortcomings of this most practical arrangement exist. The steep potential gradient at the root of the left arm[4] renders left arm coefficients highly variable from one individual to another, depending in part on left shoulder structure. The situation is similar to that which would be found if a large, variably shaped electrode were placed on an ill-defined region of the precordium. Moreover, changes in dipole location from one individual to another introduce errors of substantial amounts in all electrodes.[9] An improved system may be designed by avoiding the use of the left arm, as is done here. Vulnerability to dipole location errors is not circumvented easily, however, since effects of dipole location on body surface potentials are very pronounced. Furthermore, limb and back electrodes are about as insensitive to dipole location effects as any body surface points. Dipole location effects can be reduced substantially by increasing the number of carefully selected electrodes and interconnecting them in a fashion suitable to achieve compensation. For example, the SVEC III system of Schmitt and Simonson[7] utilizes this first-derivative compensation principle, but requires 14 electrodes. The system proposed here, shown in figure 1, applies this principle, using a total of 7 electrodes, 3 more than the minimum theoretic number, in order to avoid strong dependence on dipole location.

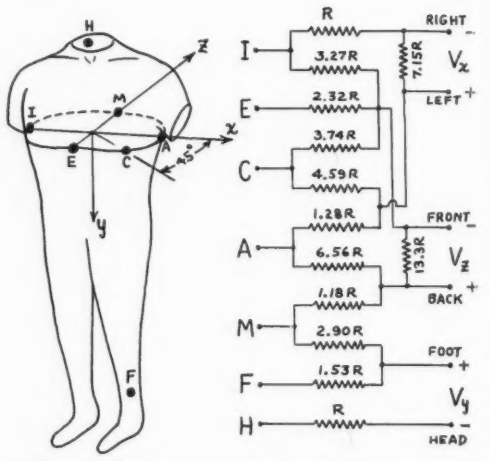

FIG. 1. The seven electrodes of this system of vectocardiography are shown at the left affixed to a human subject. Five electrodes A, C, E, I, M are located at the same transverse level (approximately the fifth interspace), H is on the back of the neck, and F is the standard left leg electrode. Wires joining these electrodes may be connected directly to corresponding points of computing and compensating networks (right), the outputs of which are three potential differences V_x, V_y, and V_z which are proportional to dipole components p_x, p_y, and p_z, respectively, with equal standardization factors. The entire system may be arranged to feed an ordinary vectorcardiograph but the shunt resistors 7.15 R and 13.3 R might require modification (see text). Effective resistance from any of the six output terminals in any path toward the subject has been designed to be equal to R, thus enabling common-mode rejection of 60 cps interference. Lead length from network outputs to vectorcardiograph should be held to a minimum.

In applying this system, the transverse level of the ventricles may be taken as the fifth interspace, or it may be determined more precisely for exacting studies by electrical technics described in Appendix I. Electrodes are placed at this transverse level at the front (E) and back (M) midlines, at right (I) and

eft (A) midaxillary lines, and at an angle of 5 degrees (C) between front midline and left midaxillary line. Letter designations of these electrodes conform to those previously published.[8, 12] The remaining two electrodes are placed on the left leg (F) and on the back of the neck (H). Potential differences among these 7 electrodes do not yield pure dipole components, but suitably weighted combinations produce accurate orthogonal dipole components for a wide range of dipole locations. The simplest networks to accomplish this are shown in figure 1. Three potential differences V_x, V_y, and V_z, very nearly proportional to each of the dipole components p_x, p_y, and p_z, are delivered with equal relative standardization for convenience in subsequent amplification in the vectorcardiograph. A description of each component follows.

Right-to-left Component, p_x. The potential difference V_x, derived from electrodes A, C, and I as shown in figure 2, appears between electrode I and a junction of 2 resistors joining A and C. Representation of electrodes A, C, and I in image space for a typical dipole location is also shown in figure 2 where the image vector for V_x is displayed in geometric terms. One role of electrode C is to introduce a correction for the backward slant of the image line from I to A by about 13° for this dipole location. Since the V_x image vector is parallel to the x-axis, the potential difference V_x is proportional to p_x for this dipole location. The relative amplitude of the V_x image vector is 174 units without the attenuating resistor 7.15 R shown in figure 1. This shunt resistor diminishes the amplitude of V_x by a factor of 1.28, which reduces its image vector to the same length as that for V_y, inherently the smallest amplitude lead. This electrode arrangement not only produces an image vector parallel to the x-axis for this particular dipole location, but maintains this property with good accuracy in both length and angle for a substantial range of different dipole locations because of the choice of electrode sites and the way in which electrode potentials are combined.

Front-to-back Component, p_z. The potential difference V_z, derived from all five electrodes at the transverse level A, C, E, I, and M as

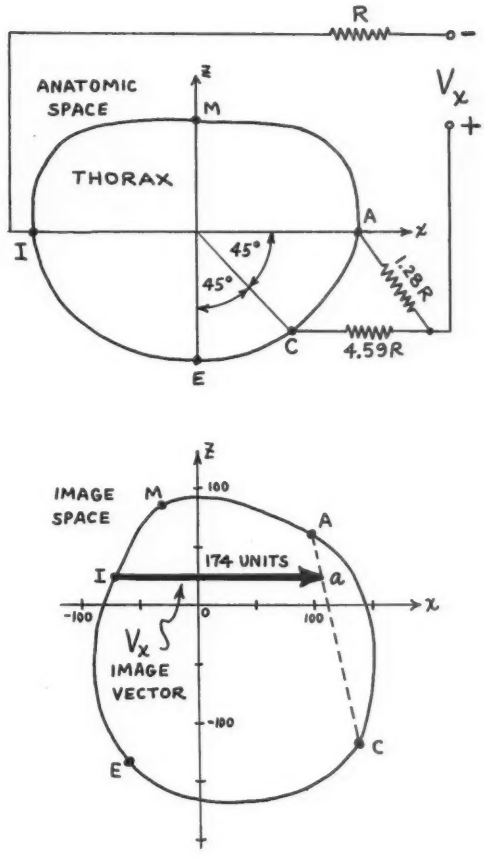

FIG. 2. Details for right-to-left component, p_x. Three electrodes, A, C, and I at the transverse level are utilized to produce V_x whose image vector is parallel to the x-axis. It is assumed that the three image points corresponding to anatomic points A, C, and I lie in the xz-plane of image space and hence have negligible contribution from p_y. This will be very nearly true if the anatomic transverse level coincides with the equivalent dipole location. The tip a of the image vector divides[17] the dotted line from A to C in image space in accordance with Aa/Ca = 1.28 R/4.59 R. Normalized data for this image loop may be found elsewhere[12] under dipole location 22. The function of resistance R is to equalize resistance levels for combating 60 cps induced in the subject.

indicated in figure 3, appears between a junction of two resistors joining M and A, and a junction of 3 resistors joining I, E and C. Five electrodes were found essential to obtain an anteroposterior lead of comparable reliability

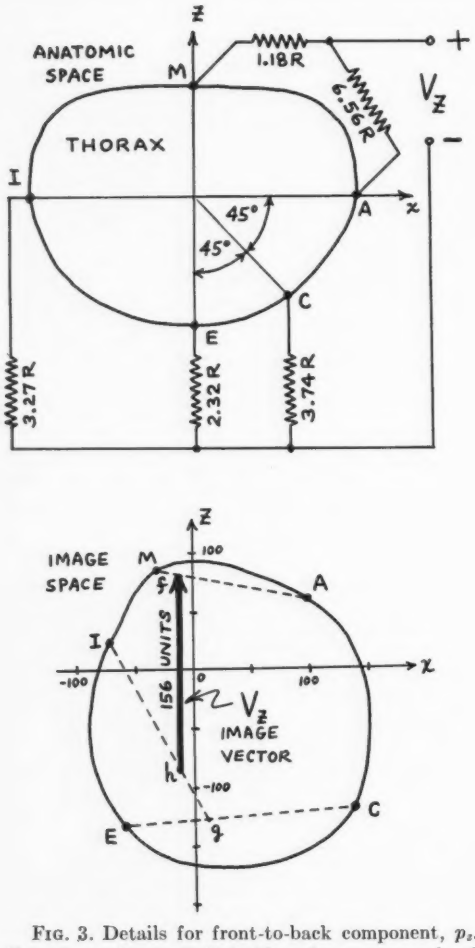

FIG. 3. Details for front-to-back component, p_z. Five electrodes A, C, E, I, M at the transverse level are utilized to produce V_z whose image vector is parallel to the z-axis. It is assumed that the 5 image points lie in the xz-plane of image space. The tip f of the image vector divides[17] the dotted line from M to C in image space in accordance with $Mf/Af = 1.18\ R/6.56\ R$. The tail h of the image vector is at a point within the triangle formed by image points I, E, C, which may be obtained as follows: join I with point g which is located along the EC line in accordance with $Eg/Cg = 2.32\ R/3.74\ R$. Point h is found along the line Ig in accordance with $gh/Ih = 3.74\ R\ (2.32\ R)/3.22\ R\ (2.32\ R + 3.74\ R)$. Proof of this construction is available on request from the author. Image loop and dipole location are the same as in figure 2. Resistance levels of the 2- and 3-resistor junctions (as seen from V_z) have been designed to be each equal to R to counteract 60 cps interference.

and quality to the other 2 leads of this system. Omission of any one of these electrodes (with suitable redesign of the networks to give a pure lead for a typical dipole location) results in significant impairment of performance in terms of vulnerability to dipole-location changes. Representation of these 5 electrodes in image space for a typical dipole location is also given in figure 3, where the image vector for V_z is shown in geometric terms. Clearly the influence of electrode A is slight, since it is weighted by only 18 per cent of the contribution of electrode M to the 2-resistor junction and again electrode C serves in part as a correction electrode (though more influential than in the p_x lead), since it is weighted least of the 3 electrodes feeding the 3-resistor junction. The V_z image vector being parallel to the z-axis indicates that potential difference V_z is proportional to p_z for this dipole location. The relative length of the V_z image vector is 156 units, without the attenuating resistor 13.3 R shown in figure 1. This shunt resistor effectively reduces the length of the V_z image vector by a factor 1.15, which equalizes it to the V_y image vector.

Head-to-foot Component, p_y. The potential difference V_y, derived from electrodes H, M, and F (fig. 4), appears between electrode H and a junction of two resistors joining M and F. Since the ratio of resistances joining M and F is 1.9 to 1.0, M may be looked upon as introducing a backward correction to the H to F potential difference. Representation of these three electrodes in image space for a typical dipole location is also shown in figure 4 in frontal and left sagittal views, where the image vector for V_y may be seen in geometric terms. The role of electrode M is clearly displayed in the sagittal view, where it can be seen to correct for the more forward location of electrode F, the angle of correction being 8° for this dipole location. Since the V_y image vector is parallel to the y-axis, the potential difference V_y is proportional to p_y for this dipole location. The relative length of the V_y image vector is 136 units, the smallest of the three, and is therefore unattenuated (fig. 1). This lead determines the amplitude level of the system

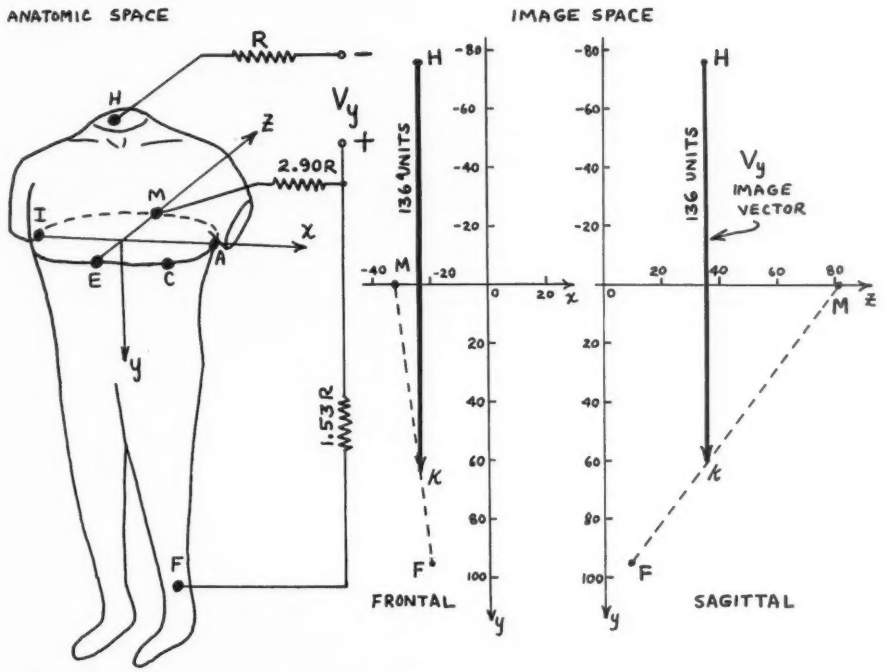

FIG. 4. Details for head-to-foot component, p_y. Three electrodes H, F, M are utilized to produce V_y whose image vector is parallel to the y-axis. The tip k of the image vector divides[17] the dotted line F to M in image space in accordance with $Fk/Mk = 1.53\ R/2.90\ R$. Data for these image points may be found in a previous publication[8] which is very nearly the same dipole location as in figures 2 and 3. The scale of the image coordinates is different from that in figures 2 and 3. The function of resistor R is to equalize the resistance level with that of the positive side of V_y, a necessary practical condition to achieve adequate 60 cps rejection.

that provides larger potential differences than obtained in most other systems of vectorcardiography.

ELECTRODE PLACEMENT

Great care must be exercised in electrode placement to take full advantage of the accuracy capabilities of the system and its invulnerability to dipole location.

Ventricle Level. For ordinary clinical routine use the transverse level of the ventricles may be taken as the fifth interspace (at the sternum). Some error may be introduced using this level, but it is usually within 1 inch of the correct level. For precise determination of the electrical level of the ventricles, the technic given in Appendix I may be employed. Fluoroscopic estimate of the anatomic center of the ventricular mass is often too high because the diaphragm obscures an uncertain portion of the ventricles. Electrodes A, C, E, I and M are all located at precisely the same anatomic level. When the subject is capable of standing, the level may be marked around the chest by the use of a string with a weight on the end (plumb bob) adjusted in length so that the weight just touches the floor at various points around the steady subject.

Angular Locations of Chest Electrodes. Electrodes E and M are placed exactly on the front and back midlines, respectively. Electrodes A and I are placed on the left and right midaxillary lines, respectively. The meaning of midaxillary line, as used here, is a line passing exactly through the axilla and parallel to the central axis of the trunk. The vertical

plane containing A and I is typically closer to the back than to the precordium, often cutting the thorax in the ratio 1.2:1.

Various types of chest protractors may be devised that permit the location of electrode C to be established at an angle of 45 degrees between electrodes E and A. This location is often deceptive because of precordial contour, and anatomic distances on the body surface from A to C and from C to E are usually unequal.

Head and Foot Electrodes. Electrode H is placed on the back of the neck 1 cm. to the right of the back midline at a level corresponding to the extension of the top shoulder line across the back. Its location is not especially critical. Electrode F, least critical of all, is at the standard location of currently used LL electrode, on the left leg, between the knee and ankle.

Theoretic Performance

Basic assumptions underlying this system of vectorcardiography are: (1) ventricular depolarization may be represented at each instant of time by an equivalent dipole that is variable in strength and orientation but is fixed at a single (but generally different) anatomic point for each individual, and (2) the medium in which heart currents are produced is homogeneous, resistive, and linear for all individuals with boundaries the same as that of the individual torso shape. These assumptions have been discussed in detail[3] and tested experimentally.[3-5, 12] As a result of this and other unpublished work, it is expected that a theory based on these assumptions will be accurate to about ± 15 per cent.

With these assumptions, the relationship between the potential at any boundary point and an internal dipole of any location may be determined experimentally by homogeneous, three dimensional torso models. Such data have been published elsewhere[2, 9, 10] including complete results for the entire torso surface.[8] The influence of torso shape has been found to be less than 10 per cent for most subjects, including male and female, except for absolute amplitude.[2, 8, 9, 10] A typical dipole location for ventricular depolarization is 9.4 per cent of the thorax width to the left of the vertical plane containing electrodes E and M, 14.8 per cent of the thorax depth forward of the vertical plane containing electrodes A and I, and at the level of the fifth interspace. This is very close to a dipole location designated as 2 in a previous publication,[12] for which complete model data have been presented.[8] Because this location is nearly at the center of results obtained in both normal persons[13] and patients whose electrical ventricle locations have been determined by actual experiment, it is taken as the design center for this system of vectorcardiography. For this typical dipole location unipolar potentials[2, 8, 12] at the seven electrodes of this system and rectangular components of the internal dipole are related by:

$$\begin{aligned} V_A &= 95\ p_x + 58\ p_z \\ V_C &= 131\ p_x - 113\ p_z \\ V_E &= -60\ p_x - 130\ p_z \\ V_M &= -32\ p_x + 80\ p_z \\ V_I &= -71\ p_x + 21\ p_z \\ V_H &= -24\ p_x - 76\ p_y + 35\ p_z \\ V_F &= -21\ p_x + 91\ p_y + 11\ p_z \end{aligned} \tag{1}$$

where coefficients are given in the same relative units defined elsewhere.[12] It is assumed here that the transverse level is correct and, therefore, that coefficients of p_y are small compared with those of p_x and p_z for the 5 transverse level electrodes. With these relationships it is possible to demonstrate that the networks of figure 1 result in the production of 3 essentially pure dipole components with equal standardization factors. Circuit equations for the 3 output voltages applied to the vectorcardiograph are, in general, for any R

$$\begin{aligned} V_x &= 0.610\ V_A + 0.171\ V_C - 0.781\ V_I \\ V_y &= 0.655\ V_F + 0.345\ V_M - 1.000\ V_H \\ V_z &= 0.133\ V_A + 0.736\ V_M - 0.264\ V_I \\ &\quad - 0.374\ V_E - 0.231\ V_C \end{aligned} \tag{2}$$

and are most conveniently obtained by node analysis[14] of the networks of figure 1. Inserting the potentials of Equation (1) into Equation (2) results in

$$\begin{aligned} V_x &= 136\ p_x - 0.2\ p_z \\ V_y &= 136\ p_y - 0.8\ p_x - 0.2\ p_z \\ V_z &= 136\ p_z \end{aligned} \tag{3}$$

Thus it can be seen in mathematical terms that each of the 3 potential differences for this dipole location is essentially proportional to only 1 of each of the 3 dipole components, and that the proportionality factors are the same for each lead.

A fundamental advantage of this system is revealed when data for a variety of different dipole locations are applied. Indeed, the system has been deliberately devised to be relatively insensitive to dipole location and, as such, surmounts a major defect of most systems. To illustrate, consider the influence on V_x of shifting the dipole to location 04, which is 2 cm. forward and 2 cm. rightward of the design-center location 22, a total shift of 2.8 cm. Electrode A, C, and I potentials are then given by[12]

$$\begin{aligned} V_A &= 71\ p_x + 68\ p_z \\ V_C &= 161\ p_x - 57\ p_z \\ V_I &= -74\ p_x + 43\ p_z \end{aligned} \qquad (4)$$

which differ considerably from those in Equation (1). Yet the V_x expression of Equation (2) still yields a faithful result: $V_x = 129\ p_x - 1.9 p_z$. The relative amplitude has been reduced by about 5 per cent from 136, and the angle error is $\tan^{-1}$ (1.9/129) = 0.8°. In similar fashion, dependence on dipole location can be calculated for the other potential differences V_y and V_z. For dipole locations within a cube 4 cm. on a side that is centered on location 22, it is found that image vectors associated with V_x, V_y, and V_z undergo length changes of about ±9 per cent and angle shifts of ±2°. For a cube 5 cm. on a side, length variations are ±20 per cent and angle shifts are ±5°. The latter volume was found to encompass 90 per cent of 40 patients with assorted heart disease whose ventricle centers were determined precisely by experiment.[5] Thus, deviations owing to individual location of dipole are usually comparable to the accuracy with which model data apply to the human subject. Deterioration in accuracy with commonly used systems of vectorcardiography when dipole location is shifted is very substantial in the range for which this system shows good performance.[9] Although this system does tend to become less accurate outside the specified 5 by 5 by 5 cubic centimeter volume, other systems become far worse.

It is of course tacitly assumed in these calculations that the transverse level at which electrodes A, C, E, I, and M are located on the subject is not seriously in error. It is noteworthy in Equation (2) that coefficients in each equation add up to zero. This is a network property resulting from equalizing resistance levels, but also indicates that if each chest electrode has about the same amount of potential traceable to p_y, a condition which is approximated if *all* chest electrodes are at a slightly incorrect level, then p_y tends to cancel out of V_x and V_z.

Practical Considerations

Several practical points based on experience with hospital patients deserve mention.

1. *Electrode Attachment.* It has been found most convenient to use a standard perforated rubber belt to hold the 5 chest electrodes. Commercially available precordial electrodes may be inserted under the belt at locations A, C, and I. Modified precordial electrodes with a straight rod perpendicular to the disk slide through an appropriate hole in the belt for locations E and M. The rod is long enough so that spacers can be slipped onto the rod and under the belt to hold electrodes firmly against the skin despite hollows in body contour frequently encountered. Electrode H consists of a flat precordial type electrode disk; it is affixed with adhesive tape. As is true in all systems, a ground electrode is required. This may be attached to any of the 3 unused limbs, such as the right leg.

2. *Female Subjects.* In female subjects, electrode C has some unavoidable error when the transverse level of the ventricles does not fall above or below the left breast. This error is not acute because electrode C serves as a correction for V_x, is weighted by about 27 per cent in its contribution to the three resistor junction of V_z, and does not affect V_y at all.

3. *Subject Posture.* Because amplitudes of potential differences V_x, V_y, and V_z are larger than those obtained in presently used systems of vectorcardiography, it has been possible

to study subjects of all ages in the sitting position with little disturbance from muscle tremor.

4. *Skin Treatment.* The network of resistors (fig. 1) may be connected directly to the subject, but it is necessary to rub the skin, so that resistance beneath the electrode is small compared with the input resistance to the network. Otherwise electrical errors are encountered. This problem is similar to the skin resistance problem[15] recognized in connection with the Wilson central terminal, and is present in any system that employs resistance networks. Hence, the choice of R (which sets the entire impedance level of the networks) is important. The value of R should be as high as is consistent with 60 cps. disturbances, desirably 100,000 ohms and not less than 25,000 ohms. The skin should be rubbed under each electrode until a resistance less than $R/10$ is achieved between any two electrodes (this may be measured roughly by using a common ohmmeter). If R = 50,000 ohms, the $R/10$ result (5000 ohms) is easily achieved with moderate rubbing which typically gives 3000-ohms resistance. If R is too small, extremely brisk rubbing is required, which is quite inconvenient, time consuming and uncomfortable.*

5. *Vectorcardiograph Input Resistance.* The input grid resistors (if any) of the amplifiers to which V_x, V_y, and V_z are delivered must be taken into account if standardization factors are to be precisely equalized. Figure 1 portrays conditions for an infinite input resistance, often approached in practice. If amplifier input resistances are each equal to KR, where K is any constant, then the shunt resistance required across V_x is given by $7.15\ KR/(K + 2)$. The shunt required for V_z is 1.86 times this value. For example, suppose the amplifier input resistance is 15 times R. Then with K = 15 a shunt value of 6.31 R is calculated for V_x (instead of 7.15 R) and a shunt of value $1.86\ (6.31\ R) = 11.8\ R$ is needed across V_z (instead of 13.3 R).

* The problem of skin resistance may be circumvented by feeding electrode potentials directly into cathode followers and applying their outputs to the resistance networks. It is necessary to use direct current for the filaments, and coupling capacitors (with suitable discharge provisions) should be incorporated to block the unequal direct voltages of V_x, V_y, and V_z from the vectorcardiograph input circuits.

Discussion

Perhaps the most striking gross feature of the system proposed here is the use of 3 precordial electrodes. This is justified by numerous experiments on many normal[13, 16, 17] and abnormal[5, 16] subjects who have given consistent and precise evidence that the dipole representation is applicable to an accuracy of 85 to 95 per cent for the precordium. The use of precordial electrodes for spatial vectorcardiography is not new. Precordial leads V_2 and V_6 have been advocated,[18, 19] a group of 4 electrodes on the precordium has been proposed,[7] and other investigators[20] have used precordial electrodes of different kinds in their systems.

Advantages and disadvantages of this system of vectorcardiography are summarized below. The basic theory underlying this system is soundly supported by experiment for the QRS complex to an accuracy of about ±15 per cent, while other systems in current use are subject to sizable known errors in both principle and practice. Torso-shape influence is corrected by model coefficients that vary by less than 10 per cent for a wide range of body builds. Effects of individual variations in left arm coefficients are avoided by excluding the left arm. Insensitivity to individual variability in dipole location is accomplished by choice of electrode sites and processing of electrode potentials in compensating and computing networks. Thus, a major shortcoming of common systems of vectorcardiography is overcome, without the need of determining the actual location of the dipole. For dipole locations within a cube 5 cm. on each side centered on a typical dipole location, image vectors remain accurate within ±5° in angle and ±20 per cent in length. Individual variability of anatomic heart orientation may be overcome, as in all systems, by studying the spatial loop in its own frame of reference rather than in terms of projections on fixed anatomic axes. The number of electrodes, while three more than the minimum theoretic requirement, is

not excessive and is less than the total number of electrode sites used in routine clinical electrocardiography. Yet just as much and even more information may be expected. Procedures involved in applying this system can be reduced to a routine requiring about 15 to 20 minutes per subject. Potential differences derived from the body surface sometimes approach twice the size of systems that employ "remote" electrodes, and represent a marked advantage in combating muscle tremor and 60-cps interference. Moreover, subjects may be studied in the sitting position, which is often a convenience impossible in other systems because of excessive muscle tremor. Electrode sites should be rubbed adequately in this system to avoid electrical errors. This disadvantage, which is minor if R is 50,000 ohms or greater, may be overcome by use of cathode followers, which have been found to be practical in this application. Cost of equipment to implement this system is not substantially different from any other system of vectorcardiography. Input leads and networks, which can be adapted to existing equipment, constitute a small percentage of total equipment cost. Potential differences representing 3 orthogonal components are produced with equal standardization factors for convenience in amplification. While electrode location is critical in this system, this is partially offset by pooling various electrode combinations. Moreover, electrode placement is critical in many other systems of vectorcardiography, and is not so precisely specified. Preliminary studies indicate that reproducibility comparable to beat-to-beat variations can be achieved, provided care is exercised in electrode placement.

A system whose stated performance compares closely to that described here is the SVEC III system.[7] The system proposed here appears to have a basic advantage over SVEC III because the left arm is not employed and, perhaps of most practical significance, the SVEC III system uses a total of 14 electrodes, twice the number required here.

Results obtained from the proposed system should not be expected to differ qualitatively in many cases from those obtained with standard electrocardiographic or other vectorcardiographic systems. For example, leads I and V_5 or V_6 are usually qualitatively similar to V_x, V_F (or aV_F) is often similar to V_y, and either V_1, V_2 or V_3 usually resembles $-V_z$. However, the main purpose of devising a more accurate system is to enable quantitative explorations; and quantitative differences between results of this system and those of other methods are enormous, amounting to several hundred per cent in amplitude and drastic differences in shape, timing and angle. An example is given in figure 5. It is believed that a more accurate system such as the one described will reveal new invariants not heretofore discernible, if indeed they are there to be found.

Vectorcardiograms (fig. 5) obtained in November 1955 enable comparison between results of the proposed system and those of the commonly used Wilson tertrahedron, for a normal subject. Absolute accuracy for the QRS complex may be judged from results of an accurate research determination carried out on the same subject in May 1954.[12] In the research determination, dipole location was established by 11 cancellation experiments[12] after which dipole components were obtained using 18 different leads dictated from torso-model results as previously described in detail.[3] Total time required for a research determination of this kind is typically 30 hours. Vectorcardiograms obtained routinely in 15 minutes by use of the presently described system are seen to agree with the research determination within the stated accuracy of the system, while the Wilson tetrahedron results contain sizable quantitative errors, most glaring of which is in the front-to-back component, p_z. This particular defect, often found with the Wilson system, is traceable in part to characteristics of the left arm which, for this subject, are known to contribute substantially to discrepancies between the two systems. The accurate p_z obtained in the proposed system in itself represents a major stride forward. There are many other known causes for disagreement; for example, exaggeration of the head-to-foot component, p_y, in the Wilson

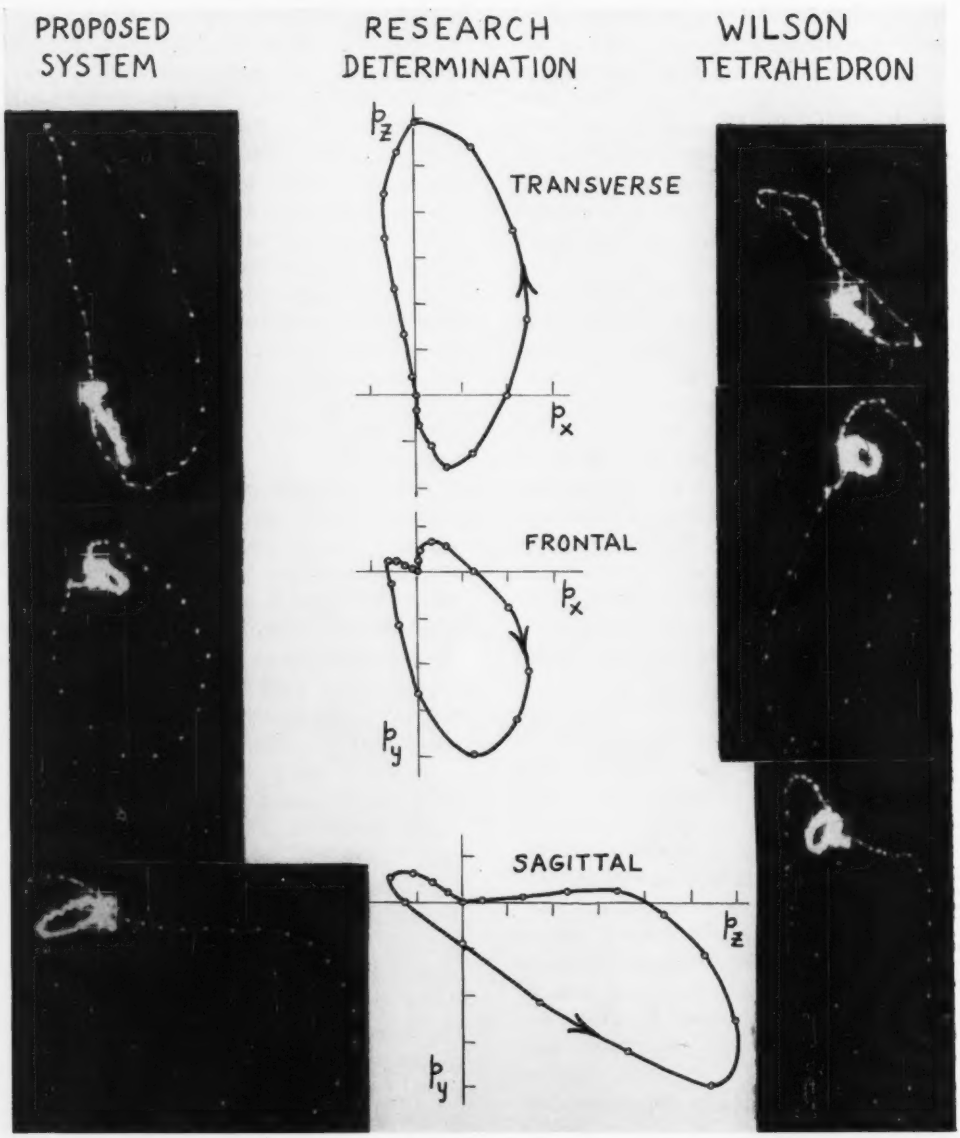

FIG. 5. Shown in the center column are previously published[1] projections of the QRS loop of a normal male subject that were determined by elaborate research technics.[3] Vectorcardiograms of the proposed system (left) are seen to be in close agreement while the Wilson system (right) contains substantial errors. Timing markers in records are spaced 2.5 milliseconds apart; bright spots occur immediately after blanked portions of the trace and reveal direction of inscription. Points on research determination are spaced 5 milliseconds apart. Rectangular grid-line spacing on records is 0.1 inch. Standardization employed in the proposed system was 1.0 in/mv. for all three components. The customary standardization factors for the Wilson tetrahedron system were employed: 1 in/mv for lead I, 1.2 in/mv. for V_B and 1.7 in/mv. for V_F. Standard electrocardiograms for this subject may be found elsewhere.[3] Records were obtained through the courtesy of the Provident Mutual Life Insurance Company, with research equipment of Dr. Paul H. Langner, Jr.

system is a characteristic that has been emphasized elsewhere.[6, 10]

While this system is soundly supported by experimental evidence for the QRS loop, there is less evidence concerning its performance with T loops and no evidence regarding P loops. It may be satisfactory for T loops because T waves cancel[21] and ventricular repolarization is representable by a fixed-location dipole. The insensitivity of this system to dipole location would then result in accurate T loops, provided the center of T-wave activity does not differ too much from that of the QRS complex.

For completeness and historic interest it should be mentioned that an accurate central terminal representing the dipole midpotential may be devised using the chest electrodes of this system. However, no such terminal is necessary for vectorcardiography and, furthermore, such a terminal cannot provide basic information not already present in the dipole components. One terminal representing the dipole midpotential more accurately than the Wilson central terminal may be formed as a junction of 3 resistors joining electrodes E, C, and M with resistance ratios $R_E/R_C = 1.45$ and $R_C/R_M = 2.82$. Another terminal at nearly the same potential may also be formed by the junction of 3 resistors joining electrodes A, C, and I with resistance ratios $R_C/R_I = 3.08$ and $R_A/R_C = 1.5$. These junctions are somewhat insensitive to dipole location, as can be shown by analysis of published image loops,[12] but they do not shift concordantly with dipole location. Potential difference between the 2 junctions on normal subjects is typically 0.13 ± 0.08 mv. provided the electrode level is correct.

Summary

1. An accurate system of spatial vectorcardiography employing 7 electrodes (3 on the precordium) in combination with computing networks is practical for clinical use, and enables quantitative analysis of electrocardiographic potentials.

2. Advantages of this system include a theoretic basis (tested by experiment) accurate to ± 15 per cent, corrections for torso shape, avoidance of left arm, insensitivity to individual variability of ventricle location, reduced muscle tremor interference, rapid application, and cost comparable to other systems. Disadvantages are critical electrode placement and requirement of low skin resistance (unless cathode followers are employed).

3. For heart dipole locations within a cube 5 cm. on a side centered on a typical ventricle location, image vectors remain accurate to within $\pm 5°$ in angle and ± 20 per cent in length.

4. Precise designations for electrode locations and many practical considerations are discussed. Theoretic design and performance are also included.

5. A novel technic for determination of the electrical level of the ventricles is offered as an optional procedure.

6. Two different 3-resistor terminals representing the dipole midpotential are described.

Appendix I

Experimental Technic for Determination of Transverse Level of Equivalent Dipole of the Human Heart

The transverse level of electrodes A, C, E, I and M is important in influencing the accuracy of dipole components derived from this system of vectorcardiography. Although the correct level is usually found within 1 inch of the fifth interspace, there are sometimes individual exceptions. Moreover, for precise research measurements it is desirable to be as certain as possible that the level selected for the chest electrodes is correct.

A novel three-step technic utilizing a triple-electrode assembly may be used to determine this level precisely in a rapid manner. The basis of the method resides in a property of the image surface in the region corresponding to the precordium. Over this region the outward bulge of the image surface is very pronounced because of the leftward and forward anatomic location of most human hearts.[8] The level at which this bulge is greatest corresponds to the desired electrical level and, in a torso model, is the level at which the internal dipole is located.[12] The objective of the method is to determine the level of maximum bulge in image space.

The electrode assembly, shown in figure 6, is utilized in the 3-step procedure below. In all cases the electrodes are always aligned with the intersection on the precordium of a plane containing the vertical central anatomic axis of the subject.

Step a. Place electrode 2 directly over the heart at the level of the fifth interspace with electrode 1

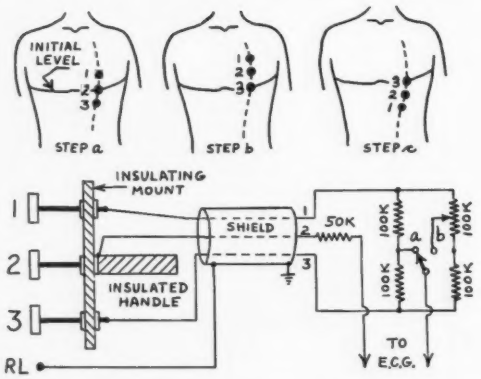

FIG. 6. The three precordial locations of electrode assembly in steps *a*, *b*, and *c* of heart level determination are shown along with electrode assembly and associated circuit and switching arrangement. Electrode 2 level in step *a* is tested for correctness by this procedure. The line along which electrodes are placed is not exactly vertical (see text). Electrodes are ½-inch diameter disks spaced exactly 1 inch apart. A ground electrode is affixed to the subject's right leg. The function of the 50,000-ohm (50 K) resistor is to equalize resistance levels as seen from the electrocardiograph.

above electrode 2 (Fig. 6, step *a*). (In female subjects a line passing just to the right or left of the left breast may be used.) With switch in position *a*, observe (and record, if desired) the shape of the QRS complex and note its amplitude.

Step b. Move the electrode assembly up by exactly 1 inch as shown in figure 6 (Step *b*), so that electrode 3 occupies the spot formerly taken by electrode 2. With switch in position *b*, vary the 100,000-ohm potentiometer until the QRS complex has approximately the same shape as observed in step *a*; note its amplitude.

Step c. Rotate the electrode assembly by 180 degrees and replace electrode 3 in the same location as in step *b* (see fig. 6). Observe the shape and amplitude of the QRS complex with switch remaining in position *b* and with no alteration of the potentiometer.

If the waveshape in step *c* is in reasonable agreement with those of steps *a* and *b*, the initial level at which electrode 2 was placed is correct, usually to within ±¼ inch. If the waveshape shows decidedly poor agreement, repeat the entire 3-step procedure starting at a different initial level. Amplitudes of the complexes often can serve as a guide in selecting a new trial level, since the QRS amplitude is frequently (but not invariably) largest at the level of maximum bulge in image space. Hence, the new level tried should be shifted toward the direction of the larger complexes.

This procedure was developed on a sound theoretic basis in terms of properties of dipole potentials in 3-dimensional torso models. Space does not permit a description of the underlying theory.

Several practical points deserve mention. The person holding the insulated handle of the electrode assembly should be connected to ground by means of a leg electrode to minimize 60 cps interference, if it is encountered. Before electrodes are applied, rub the skin along the line of the electrodes a total distance of 4 inches symmetrically about the initial level. The electrode line on the body should be wiped clean before each trial, and contiguity of electrode paste must be avoided. If complexes are too small in amplitude, the electrode line along which the determination is made may be shifted toward the midline or toward the left side. Because the method is extremely sensitive in most subjects, a small error in initial level results in a pronounced disagreement in step *c*. Therefore, waveform agreement in the 3 steps need not be perfect to obtain good accuracy. Three trials are usually the maximum number required to arrive at a final result, once the technic has been mastered. An ordinary electrocardiograph or one input of the vectorcardiograph may be used to observe complexes. This method has been applied successfully in over 100 hospital patients. A typical time required for each subject is about 5 minutes.

ACKNOWLEDGMENT

Active interest shown by Dr. G. E. Seiden and cooperation of Dr. C. F. Kay are gratefully acknowledged.

SUMMARIO IN INTERLINGUA

1. Es presentate un accurate systema de vectocardiographia spatial que es de valor practic in usos clinic. Illo emplea 7 electrodos (3 al precordio) in combination con retes de computation. Illo rende possibile le analyse quantitative de potentiales electrocardiographic.

2. Le avantages del systema include un experimentalmente verificate base theoric con un exactitude de ±15 pro cento, correctiones pro le configuration del torso, evitation del bracio sinistre, non-influentiabilitate per variationes individual del location ventricular, reducite interferentia per tremores muscular, rapide applicabilitate, e un costo comparabile al costo de altere systemas. Le disavantages es le importantia critic del placiamento del electrodos e le necessitate de basse resistentias cutanee (excepte si sequitores cathodic es empleate).

3. Pro locationes de dipolo cardiac intra un

ubo de 5 cm super un latere centrate verso un ypic location ventricular, le vectores de magine remane accurate intra ±5° in angulo ± ±20 pro cento in longitude.

4. Es discutite precise designationes pro ocationes electrodic e multe considerationes ractic. Theoric structura e efficacia es etiam ractate.

5. Un nove technica pro le determination del nivello electric del ventriculos es offerite pro uso optional.

6. Es describite 2 differente terminales a 3 resistentias representante le mediepotential dipolar.

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CLINICAL CONFERENCE

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Rupture of the Aortic Valve

By WILLIAM L. PROUDFIT, M.D., AND LAWRENCE J. MCCORMACK, M.D.

RUPTURE OF THE AORTIC VALVE has been recognized in the past, but interest in the diagnosis has been purely academic. Clinical interest in this rare lesion has been stimulated by the recent development of a surgical method of treatment. The following case is presented and discussed to emphasize the clinical signs of rupture of the aortic valve.

CASE PRESENTATION

A 56 year old city fireman had been well until he was in an automobile accident on August 5, 1950. At that time his blood pressure was found to be elevated. On Sept. 7, 1950, physical examination revealed no significant abnormalities except for a blood pressure of 180/100 mm. Hg. He remained in fairly satisfactory condition, except for elevation of blood pressure to about 200/125 mm. Hg, until May 1951, when a cerebral thrombosis occurred; recovery was fairly satisfactory.

In July 1951, a presystolic gallop rhythm was noted but no cardiac murmurs. On January 31, 1952, he was feeling quite well, but his blood pressure was 176/104 and the presystolic gallop rhythm still was present. On Sept. 19, 1952, he was next seen because of dyspnea and orthopnea of several weeks' duration. On examination, his blood pressure was 190/94, a gallop rhythm was present and, for the first time, there was a loud, musical, cooing, diastolic murmur that was best heard along the left border of the sternum. A systolic blowing murmur of moderate intensity also was present, and there was a rumbling mid and late diastolic murmur at the cardiac apex. An electrocardiogram showed only slight left axis deviation and a flat T wave in lead aV_L. The left axis deviation was less marked than that recorded on Sept. 9, 1950. On roentgen examination of the chest, the transverse diameter of the heart measured 19.6 cm. (2.6 cm. greater than two years previously), and the cardiac configuration was that of left ventricular hypertrophy.

Treatment consisting of a low-salt diet, digitalization, and mercurial diuretics resulted in prompt improvement. He remained fairly well during the following 14 months. His blood pressure varied from 126 to 190 mm. Hg systolic, and from 50 to 70 mm. Hg diastolic, and the gallop rhythm disappeared. He was last seen on Nov. 11, 1953, at which time he had no complaints. Physical examination showed no change from the previous findings and the blood pressure was 150/50. On the morning of Nov. 18, 1953, the patient was found dead in bed. He had had no complaints on retiring the previous evening.

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DISCUSSION

DR. WILLIAM L. PROUDFIT (member of the Staff of the Department of Cardiovascular Disease): The diagnosis of rupture of the aortic valve is not a difficult one to make in most cases. The cardinal sign of rupture of the aortic valve is the occurrence of a musical aortic diastolic murmur. Usually the murmur is very loud, prolonged and widely transmitted, and is accompanied by a thrill. A systolic murmur also may be present. The musical character of the diastolic murmur is a result of its being almost a pure tone—rather than a mixture of tones or a noise. The tone may be higher pitched in early diastole than in the latter part of diastole and the pitch may vary from case to case. Vibrations of 130 to 340 per second were found in the series reported by Gelfand and Bellet.[1] In our case the diastolic murmur had a frequency of about 250 cycles per second. Various descriptive terms have been applied to the murmur, most commonly, *cooing dove* or *sea gull*. The murmur bears a striking resemblance to the last 3 notes of the 5 note call of the mourning dove. However, the pitch of the birdcall is higher, the frequency being

about 470 cycles per second in the call we have studied, and the frequency is constant for the duration of the note. Frings of the Pennsylvania State University, an authority on the calls of sea gulls, points out in a personal communication that there is a variety of calls, but none of them resembles the tape-recorded sound created by the musical diastolic murmur of a ruptured aortic valve.

The musical aortic diastolic murmur is well transmitted to the cardiac apex, but Austin Flint murmurs also are common in cases of rupture of the aortic valve. The musical murmur beginning early in diastole may be heard at the apex and, in addition, there may be a low rumbling mid and late diastolic murmur, as was noted in the case just presented.

The diastolic pressure usually is low in aortic valvular rupture, and Korotkoff's sounds may be heard to zero diastolic pressure. Peripheral signs of aortic insufficiency are present when the diastolic pressure is low. It is interesting that in this case both the systolic and diastolic pressures decreased after rupture of the valve.

The prognosis of the disease is poor, and death usually occurs within a few weeks or months; occasional patients may live for many months or even several years. Congestive heart failure, which is resistant to treatment, is the principal complication and results in death.

There is no clue in the history as to an etiologic basis for rupture of the aortic valve. Syphilitic valvular disease is a predisposing factor in many cases of rupture of the aortic valve. Eversion of the aortic valve, which is indistinguishable clinically from rupture, is a complication also of syphilitic disease. Rheumatic cardiac disease rarely may predispose to rupture of the valve. Bacterial endocarditis may cause a perforation of a leaflet with ensuing traumatic rupture of the aortic valve. Spontaneous rupture of otherwise normal-appearing valves may be seen. Hypertension is a possible predisposing factor.

Rupture or eversion of the aortic valve may be accompanied by sudden onset of pain, dyspnea or shock coincident with the performance of some strenuous physical activity. Later, dyspnea due to left ventricular failure is the predominant symptom, though anginal pain may occur.

The case presented is unusual in that the initial symptoms were well controlled by treatment during the terminal 14 months of life. The cause of sudden death was not apparent.

Dr. McCormack, will you describe the findings of the postmortem examination?

Dr. Lawrence. J McCormack (member of the Staff of the Department of Pathology): The pertinent necropsy findings were limited to the heart, lungs and kidneys.

The *heart* weighed 930 Gm. There was a massive left ventricular preponderance with the apex being made up entirely of the left ventricle. Dissection of the coronary circulation demonstrated a normal distribution with some atherosclerosis producing luminal narrowing up to 25 per cent. The opened right atrium was not remarkable; the tricuspid valve measured 14 cm. in circumference and possessed normally formed, thin, pliable valvular leaflets. The right ventricle measured 10.0 cm. in depth and its wall was 4.0 mm. in thickness. The pulmonary valve measured 7 cm. in diameter and was not remarkable. The opened left atrium was smooth and thin walled. The mitral valve measured some 11.0 cm. in circumference with thin, pliable leaflets. The chordae tendineae were not remarkable. The left ventricular myocardium was pale and thickened to 2.5 cm. (fig. 1). The trabeculae carneae were flattened, and there was some

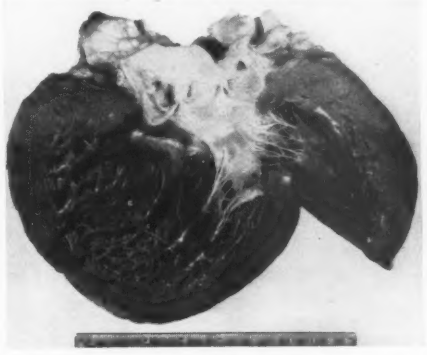

Fig. 1. Gross specimen of heart with left ventricle opened. Myocardial hypertrophy and cardiac dilatation are the prominent features.

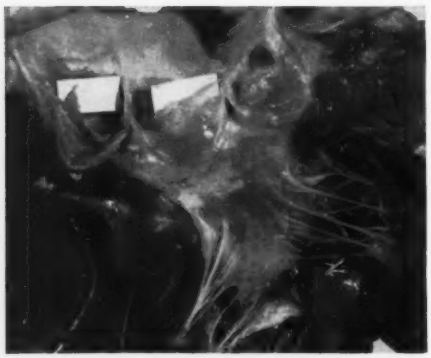

FIG. 2. Close-up of aortic valve. The anterior leaflet is fenestrated; the left semilunar cusp is both fenestrated and torn. The separated left portion (right side of photograph) points superiorly.

dilatation of the left ventricle. Just inferior to the left cusp of the aortic valve could be seen 3 transverse fibrous thickenings, measuring up to 1.0 cm. in length and 0.2 cm. in thickness. The thickenings in actuality were small cusped structures with their free margins pointing toward the aortic valve. The aortic valve measured 7.0 cm. in diameter. Its 3 cusps were equal in size. The cardiac surface of the left cusp was reddened and appeared slightly thickened. The anterior cusp showed a small fenestration near its point of union with the aorta on the left side. The fenestration measured 4.0 by 1.0 mm.; the free margin of the cusp was intact. The left cusp showed a similar fenestration but, in addition, the left point of its attachment had pulled free from the aortic annulus and possessed a bulbous enlargement at the free tip (fig. 2). Histologic preparation demonstrated an increased cellularity of the right and left cusp margins; they also were thickened by a deposition of fibrin. No disease was demonstrable in the aortic wall at the point of attachment. Sections through the thickened areas of the endocardium showed them to be composed of fibroblasts. The myocardium possessed enlarged muscular fibers, but no necrosis or fibrosis was noted.

The *lungs* were heavy, weighing 1505 Gm. The external surface was mottled gray, red and black. Palpation demonstrated some increased consistency. The cut surface was grayish red in color, and copious amounts of frothy fluid could be expressed from the surfaces. Microscopically, the lung showed a granular coagulum within many of the alveoli.

The *kidneys* were of normal size, with a combined weight of 400 Gm. Their external surfaces were finely granular and the cut section demonstrated the same fine granularity with good demarcation of cortex and medulla. The cortex measured 0.7 cm. in thickness. Histologically, the changes were limited to the medium-sized and small arterioles. The medium-sized ones showed a marked degree of intimal thickening, but the small arterioles were only moderately thickened and uniformly hyalinized.

ANATOMIC DIAGNOSES

Rupture of left semilunar cusp of aortic valve with resultant aortic insufficiency.
Cardiomegaly (930 Gm.), predominantly left ventricle.
Cardiac dilatation, acute.
Fenestration, small, anterior cusp of aortic valve.
Jet lesion, endocardium.
Trauma of aortic valvular cusps.
Acute pulmonary edema (1505 Gm.).
Arteriolar nephrosclerosis.

DR. PROUDFIT: What evidence is there that the aortic insufficiency was functionally significant?

DR. MCCORMACK: Evidences that the valvular lesion was of functional significance are several. First of all, the flailing valvular margin striking the other semilunar cusps produced a moderate degree of nonspecific endocardial reaction. The 3 cusplike structures on the endocardial wall inferior to the valve are classic for a so-called "jet" lesion and are produced by an abnormal stream of blood striking the endocardium. The massive myocardial hypertrophy seems out of proportion to the amount of hypertension the patient had and is much more consistent with the cardiac size of aortic insufficiency.

DR. PROUDFIT: It is important to recognize rupture or eversion of the aortic valve because

of the possibility of treating it effectively. Radical measures are justified because the prognosis is grave. Recently, Leonard, Harvey and Hufnagel[2] reported treatment of traumatic rupture by insertion of a Hufnagel plastic valve in the aorta, distal to the origin of the left subclavian artery. Postoperatively, the diastolic blood pressure returned to normal and the patient was able to resume his usual employment. Because a direct approach to the aortic valve for repair of the defect is not possible at the present time, the Hufnagel operation should be employed until a more satisfactory surgical treatment has been devised.

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Re-opening the Case of the Abdominal Aortic Aneurysm

By IRVING S. WRIGHT, M.D., ENRIQUE URDANETA, M.D., AND BARBARA WRIGHT, B.S.

UNTIL recent years, the problem of the abdominal aortic aneurysm* was of academic interest only. The diagnosis once established by physical examination or laparotomy was accepted with a reaction of fatalism toward the future. The rate of progress was uncertain but the life span was shortened and in some cases death occurred within a few weeks or months. On the other hand, for reasons unknown, there were patients who survived for five years or longer. There was no known treatment. It was recognized that while most thoracic aneurysms were syphilitic in origin, the greater percentage of abdominal aneurysms were on the basis of atherosclerosis. The majority of these involve the *lower* abdominal aorta, which is used in this paper to signify the portion below the renal arteries. This interesting phenomenon was clearly shown in Blakemore's[1] series of 365 cases of aortic aneurysm. Of the 192 syphilitic aneurysms, 182 involved the thoracic aorta and only 10 involved the abdominal aorta; whereas of the 143 arteriosclerotic aneurysms, 114 involved the abdominal aorta and only 29 involved the thoracic segment. Of 30 miscellaneous types including mycotic, traumatic and unclassified, 15 were thoracic and 13 abdominal in location, 2 were unclassified. The reason for this anatomic predilection has never been completely clear, but the explanation of Blakemore is worthy of careful consideration. He suggested that the explanation of the development of aneurysm resulting from atherosclerosis of the lower abdominal aorta was due to several factors:

1. Widespread atherosclerosis tends to involve the entire aorta, including the lower abdominal segment.

2. The pressure of pulse waves striking the aortic bifurcation and the iliac arteries tends to produce a reverse wave that meets the oncoming next pulse wave. This results in a hammerhead of pressure with a sideways thrust and stress on the aortic wall, which is not well supported by sheathing or surrounding tissues at this point.

3. This stress may be aggravated by the fact that the aorta is fixed at the diaphragm and by the iliac fascia. Between these two fixed points, the aorta tends to elongate with atherosclerosis. It usually deviates to the left. This bending tube tends with further strain to dilate into a fusiform aneurysm. This lack of fixation and the deviation forward also explain why erosion of the spine and radiculitis are rare in abdominal aneurysms as compared with thoracic aneurysms.

While these may be logical explanations for the location of atherosclerotic aneurysms in the abdominal aorta, they fail to explain the predilection of the spirochete for the thoracic aorta. This has been held by some to be related to the arrangements of the lymphatic system, but this must be regarded as speculation rather than fact.

With the development of surgical procedures that render the abdominal aortic aneurysm subject to attack, it seems justified to attempt a critical evaluation of the current situation.

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* This report does not include a consideration of dissecting aneurysm.

The results of surgery are striking, often spectacular, but not universally successful. Why?

This presentation attempts to examine the questions dealing with prognosis, symptoms, signs and other means of diagnosis, selection of cases, indications and contraindications, effects of location, extent and type of aneurysm, preoperative and postoperative care and surgical technics (briefly).

Prognosis. To justify this relatively radical surgery it is necessary to establish that the outlook for the patient is poor without surgical intervention and that such an approach offers a reasonable chance for improving the outlook. At present, the view is held by some surgeons working in this field that most patients have a life span of less than two years after discovery of the aneurysm. They reason, therefore, that operation is imperative and should be done with minimum loss of time, citing examples of patients who have died from rupture of their aneurysm before they could be operated upon. On the other hand, there are many internists and general practitioners who take a rather casual attitude toward these aneurysms after their discovery. They cite patients who have lived for many years with an aneurysm without much progression or rupture. It is probable that, to date, most of the series of cases reported by surgeons fail to represent the true picture in this regard, since patients who are having pain, increase in the size of the mass or other signs associated with expansion of the aneurysm are especially likely to gravitate toward the surgeon, as compared to those who are symptom free.

One of the most revealing articles in this regard is that of Estes reporting the experience of the Mayo Clinic.[2] The prognosis of 102 cases is seen in table 1. Approximately 58 per cent survived 2 years, only 19 per cent survived 5 years, and 10 per cent survived 8 years. It should be remembered, however, that the mean average of this group of patients was 65 years at the time of diagnosis, so that the expectant mortality during the subsequent years would naturally be high. Estes reported that the mortality of patients with abdominal aneurysm was consistently higher than that found in comparable groups without such aneurysms.

TABLE 1.—*Life Expectancy (Estes)*

Years	Total	Patients traced	Survival beyond period	
			Number	Per cent
1	102	91	61	67
2	84	74	43	58.1
3	74	63	31	49.2
4	62	52	14	26.9
5	46	37	7	18.9
8	25	20	2	10.0
10	11	8	0 (based on data of 8 traced cases)	

TABLE 2.—*Life Expectancy (Wright et al.)*

No. patients surviving	%	Duration in years
41	60.3	Less than 1
27	39.7	1
20	29.4	2
11	16.2	3
8	11.8	4
3	4.1	5
3	4.1	6
0	0.0	7

Total traced patients—68 (nonoperated)

In his series, the cause of death in 49 of the 64 known dead was as follows: 31 (63.3 per cent) died from rupture of the aneurysm; 18 (36 per cent) died from other causes.

In our series of 68 patients who were investigated for life expectancy, the findings are given in table 2. This shows that 39.7 per cent lived less than 1 year after the diagnosis was made. Only 20, or 29.4 per cent, were alive at the end of 2 years. Eight, or 11.8 per cent, lived 4 years, and less than 5 per cent lived 5 years. A very few of these patients may have died of causes other then their aneurysms.

These figures indicate a prognosis comparable to many forms of cancer, and the condition must be recognized as a malignant one. On the basis of these experiences, the use of a fairly radical approach seems justified, since no form of conservative therapy exerts any effect on the course of this condition. The results of surgery are discussed later.

Present Series. We have analyzed the data from 107 cases of abdominal aortic aneurysm seen at the New York Hospital during the 10-

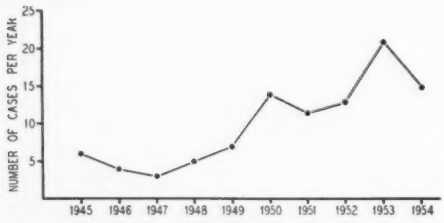

FIG. 1. Number of cases of abdominal aortic aneurysm per year at The New York Hospital.

TABLE 3.—*Ratio of Recognized Abdominal Aortic Aneurysms to Total Admissions to The New York Hospital*

Year	No. of admissions	No. of abdominal aortic aneurysms	Per cent of abdominal aortic aneurysms
1945	17,589	6	0.03
1946	19,079	4	0.02
1947	20,098	3	0.01
1948	20,457	5	0.02
1949	20,914	7	0.03
1950	21,944	14	0.07
1951	21,249	12	0.06
1952	21,500	13	0.06
1953	22,644	21	0.09
1954	22,824	15	0.07
1955		7 (incomplete)	
Total	208,298	107	0.05

TABLE 4.—*Age Incidence*

Age	No. of cases
40–49	4
50–59	24
60–69	38
70–79	34
80–89	7
Average age 66.0	

year period between 1945 and 1955 (fig. 1 and table 3). For age incidence see table 4.

Signs and Symptoms. Although signs and symptoms of this condition have been previously listed, it is believed that analyzing them in greater detail may focus attention on more precise and earlier diagnoses in the future. In addition, the present rarity of syphilis as an associated factor and other considerations may alter the findings. For example, this series was practically entirely of white patients, there being only four Negroes. There were 89 males and 18 females. In Lord's series[3] 22 out of 23 were males. Dr. Jere Lord has kindly consented to allow us to study an additional series of 23 patients, not admitted to The New York Hospital. In some respects this group is of particular interest, since patients referred to a surgeon may differ from those in a mixed hospital population.

The diagnoses in our series were made or confirmed as follows: clinically, 63; x-ray study, 48; laparotomy, 16; post mortem, 24. The diagnosis was first made at laparotomy in 5 patients and first made at postmortem examination in 20 patients.

Pain. Pain was a major complaint, but 34 patients did not suffer from it. Of the others, 27 had severe pain, 7 described it as crampy, 13 complained of rather diffuse discomfort. Many had pain or other symptoms involving more than one area. In Dr. Lord's cases, 21 out of 23 suffered from pain. This is to be expected in a selected group such as those referred to a surgeon. The distribution of pain is shown in table 5. In some cases, the pain as well as other symptoms ascribed to the aneurysm may, in fact, have been due to some other disease, so that the symptoms herein listed as due to the aneurysm are approximate rather than absolute. Symptoms are listed in table 6. Seventeen patients remained asymptomatic. In Blakemore's series,[1] 33.6 per cent and in Estes'

TABLE 5.—*Distribution of Pain*

Abdominal	54
Low back	34
Legs	13
Chest	12
Groin	7

TABLE 6.—*Symptoms*

Constipation	17
Pain	73
Anorexia	13
Vomiting	13
Dyspnea	9
Diarrhea	8
Intermittent claudication	8
Throbbing sensation	6
Unconsciousness	4

series,[2] 30.4 per cent were asymptomatic on admission.

Physical Signs. The commonest physical sign was a mass, which was noted in 65 patients. For the various locations of this mass, see table 7. In 59 cases, the masses were pulsatile. Some of these masses could be felt laterally as well as in the midline. The actual location of the aneurysm was found to be below the renal arteries in 58 cases and above the renal arteries in 12. In 15 cases, the aneurysm involved the bifurcation and proximal iliac arteries. *Nineteen patients had 31 other aneurysms in various other arteries.* Five had additional aneurysms involving the thoracic aorta. None of our patients had evidence of the rare complication of associated aneurysm of the coronary arteries reported by Rukstinat.[4] His patient died from a rupture of an aneurysm of the abdominal aorta and was found to have six aneurysms of the right coronary artery associated with marked atherosclerosis. An aneurysm of the left common iliac artery was also present, but that is not unusual. Manohar[5] reported an aneurysm of the left coronary artery complicating an abdominal aneurysm which, however, was primarily of the celiac axis, involving the celiac branches above and the superior mesenteric artery below. Death occurred as a result of a rupture between the aorta and the aneurysm. In this case, the postmortem studies supposedly established the etiology as syphilis. Physical signs of our patients are listed in table 8.

Roentgenographic Studies. In 16 cases the diagnosis was made in the course of routine abdominal x-ray examinations. In 10 cases it was made in the course of intravenous pyelogram studies. In 23 cases it was more completely delineated by aortograms. It should be mentioned that, at times, anteroposterior and lateral films of the abdomen may show the outline of the dilated aorta clearly delineated by the calcific deposits, whereas the aortogram shows only a smooth tube about the size of the aorta and without evidence of any disease. This was very definite in the case of patient G.M. (fig. 2). It was due to the formation of a firm thrombotic lining of the aneurysmal sac. In such cases the aortogram fails to be helpful, while the diagnosis may be clear on physical examination and routine x-ray studies. Aortograms are not always uneventful. There have been cases of hypersensitivity reactions to the injected substance and of local hemorrhage, although these are few.

TABLE 7.—*Location of Mass*

Umbilical area	17
Left upper quadrant	15
Epigastrium	14
Right upper quadrant	6
Left lower quadrant	6
Left flank	5
Right lower quadrant	4
Right flank	2
Hypogastrium	2
Total left side	26
Total right side	12
Total midline	33

TABLE 8.—*Physical Signs*

Mass	65
Tenderness on palpation	32
Weight loss	23
Bruit on auscultation	20
Diminished or absent pulses in groin or legs	11
Patient in shock	9
Abdominal distention	8
Edema of legs	5

The following case illustrates another type of problem.

M.B., a 64 year old, unmarried woman noticed cramps in the abdomen, especially in the lower quadrants, seven years prior to admission. She then had bloody diarrhea with 4 to 5 stools in a period of 4 hours. This was accompanied by anorexia, nausea and slight vomiting. X-ray films showed diverticulitis with fever and leukocytosis. Six years prior to admission, she had developed gnawing pain in the epigastrium that did not radiate at first but kept recurring on walking. It was unrelated to meals and relieved by the ingestion of hot water or by pressure. A pulsating mass was felt, and the diagnosis of abdominal aneurysm was made. The pain disappeared for a year, after which it recurred with the same characteristics. This kept recurring. The patient was able to continue her work as a domestic servant. Six months prior to admission the patient had an increase of symptoms with increasing anorexia

and weight loss of 10 pounds. Four months prior to admission she noticed a "pounding" sensation in the epigastrium. This progressed, becoming more severe, especially on the day before admission, when she developed marked nausea and nocturia (30 times). This patient developed the signs and symptoms of myocardial infarction, immediately following an abdominal aortogram that revealed an aortic aneurysm. She died, and autopsy showed atherosclerotic coronary occlusion with apical myocardial infarction. A second infarction, 3 by 4 cm. in size, was present in the septum. The coronary arteries were severely atherosclerotic with narrowing of the lumina to pinpoint size at numerous points. A thrombus occluded the left circumflex branch. There were aneurysms of the abdominal aorta and of the iliac arteries. An aneurysm 12 cm. in length and 5 cm. in diameter was present in the aorta between the superior mesenteric artery and the bifurcation. There were smaller aneurysms of each common iliac artery and one of each internal iliac (hypogastric) artery.

A typical case history illustrating many of the above points may be found in that of patient G.M., a 54 year old man who first developed evidence of arteriosclerosis obliterans in the right leg in 1946. A lumbar sympathectomy was performed in an Army hospital. This resulted in warming up the foot but no improvement in the claudication distance of one and a half to two blocks. X-ray films taken at that time revealed calcification of the walls of the aorta and the major vessels of both legs. No evidence of an aneurysm was noted then, nor until 1953. Meanwhile, on a conservative regimen including abstinence from tobacco, he did very well, increasing his walking distance up to one-half mile. He was carefully followed and frequently examined in detail during the intervening years. No abdominal mass was felt. In April 1953, the patient noticed the onset of recurrent night pain in the left side of the abdomen. After two weeks, a severe pain developed in the same area and, shortly after, examination revealed a peach-sized pulsating mass. X-ray examination revealed calcific deposits

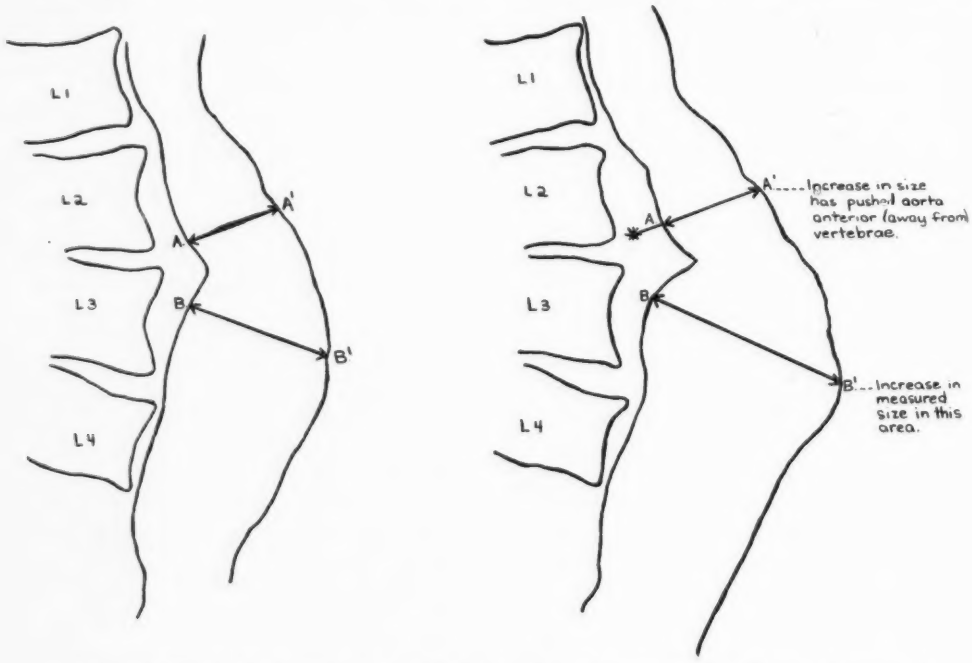

FIG. 2. Patient G. M., tracings made of calcific outlines of aorta showing evidence of increase in size of the abdominal aneurysm between Nov. 10, 1953 and June 9, 1955 (lateral view).

in the wall of the aorta outlining a dilatation mostly to the left, extending from the interspace between the second and third lumbar vertebrae to the interspace between the fourth and fifth. This was observed during the next two years. There were very few symptoms, but in June 1955 physical and x-ray examinations showed definite enlargement of the aneurysm (fig. 2). The aortogram was of little value, since it merely showed a tubular lumen of about the normal size, the remainder of the aneurysm being filled with clot (fig. 3). In this case, as in many others, the physical examination and the plain film of the abdomen were more useful than the aortogram. A transplant was decided upon, and this was performed by Dr. Edward Keefer. Aneurysms were also found in each of the iliac arteries, about 2.5 cm. in diameter and about 2 cm. below the bifurcation of the aorta. The immediate postoperative condition was satisfactory but the following day he developed respiratory distress and cyanosis. His condition deteriorated and, despite transfusions, Levophed and oxygen, he died that afternoon.

Autopsy Findings: Arteriosclerotic cardiovascular disease with resected aneurysm of the abdominal aorta, severe coronary sclerosis and diffuse myocardial fibrosis. (Patient G.M.) There was extensive atheromatosis of the upper abdominal and thoracic aorta, with some calcification and ulceration of atheromatous plaques. The lower abdominal aorta was resected and a graft inserted. The proximal anastomosis of the arterial graft was just caudal to the renal arteries, and the distal common iliac anastomoses were 3 cm. from the bifurcation of the aorta. There was only a small amount of clotted blood around the suture lines, which appeared to be intact. The lumen of the graft was patent. All the coronary arteries were calcified and their lumina narrowed by as much as 95 per cent. There was hemorrhage within one of the plaques in the right coronary artery. There were several foci of fibrosis within the myocardium; the largest measured 8 mm. in diameter and was in the interventricular septum.

The gallbladder was absent. The common duct was dilated and measured 1.8 cm. in circumference. A pyramidal stone, 5 mm. in diameter, lay in an out-pouching of the duct, 1 cm. from the ampulla of Vater. There was granularity of the ductal mucosa. The biliary system was patent.

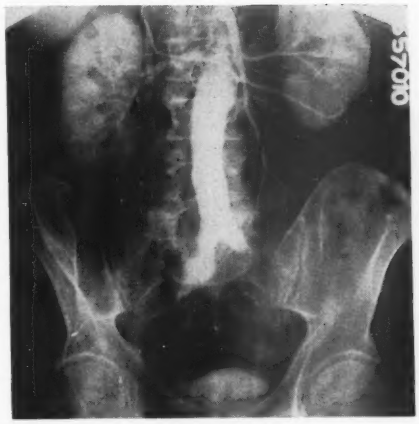

FIG. 3. Aortogram that failed to reveal actual outline of aneurysm because of laminated thrombus lining the lumen. The black line indicates the true wall as indicated by calcific deposits that were clearly seen but too fine to show on this reproduction. It shows the aneurysm in the right iliac artery, but fails to reveal the corresponding one in the left iliac artery.

TABLE 9.—*Significant Laboratory Findings*

Leukocytosis	30
Albuminuria	26
Blood urea nitrogen retention	24
Anemia (usually hypochromic)	20

Two ulcers, one adjacent to the other, were present in the left lateral wall of the duodenum 3 cm. from the pylorus. Each measured 6 mm. in diameter and 3 mm. in depth. Some of the abdominal complaints may have been due to these accessory findings.

Laboratory Findings. The most commonly encountered laboratory findings are presented in table 9. Evidence of renal disease was usually found associated with aneurysms above or involving the renal arteries. Aneurysms may dissect the walls of the renal arteries and produce renal calculi, uremia and hypertension.[6] No such cases were found in the present series from which dissecting aneurysms were excluded.

Additional Pathologic Conditions. Eighty-three of these patients had definite evidence of atherosclerosis elsewhere in their arterial system. Seventy-two had cardiovascular disease, which was predominantly atherosclerotic, with or without hypertension. Fifty-four had high blood pressure, using the upper standards of normal as 150 maximum systolic and 90 maximum diastolic. Only four had diabetes mellitus. Twenty-two suffered from gastrointestinal disease, including 7 with cancer, 5 with peptic ulcers and 3 with inflammatory reactions, such as gastritis, 4 with diverticulitis and 2 with gallbladder disease. These conditions frequently produced confusing symptomatology. Twenty-two had genitourinary complaints including 7 with cancer of the bladder, 5 with nephrosclerosis, 3 with uremia, 2 with cancer of the prostate, 3 with renal infarcts and a variety of less significant conditions. Nineteen had evidence of pulmonary conditions; 10 of these had emphysema; the others varied greatly but included 4 with cancer of the lungs. Seven had evidence of neurologic conditions, including 5 with cerebral vascular accidents and 3 with cerebral vascular disease without strokes.

Only four of these patients had serologic or other evidence of syphilis, and in only one instance was it believed that the aneurysm might have a syphilitic component. Even in this case, syphilis was believed to be of doubtful importance in reference to the development of the aneurysm. This presents further evidence of the striking trend of the decreasing significance of syphilis as a factor in the development of aortic aneurysm. The picture is not quite so clear-cut, however, in reference to abdominal aneurysm as it might appear at first glance. Although it has long been recognized, as mentioned above, that thoracic aneurysms were predominantly syphilitic, while abdominal aneurysms were less likely to be, early papers still list syphilis as a cause or contributing factor in from 25 to 75 per cent of cases of abdominal aneurysms. It is doubtful that this represents the actual facts. Careful study of these papers indicates that in many instances the mere finding of positive serologic or historical evidence of syphilis, but without histologic evidence at the site of the aneurysm, led to the conclusion that any aortic aneurysm was wholly or partly due to syphilis. In the light of present knowledge, that assumption was unjustified and led to invalid conclusions. This was especially aggravated by the fact that some of these reports came from the South, where the percentage of Negroes in the cases studied was high and where syphilis was extremely common among Negroes at that time. On the basis of pathologic findings, it appears that there has been some decrease in the number of syphilitic abdominal aneurysms but that this is much less significant than might be concluded from a casual study of the figures alone. For a review of this trend and the problems of analysis, as outlined above, the reader is referred to the papers of Kampmeier,[7] Hubeny and Pollack,[8] Scott,[9] Blakemore,[10] Estes[2] and Goldowsky.[11]

Mycotic Aneurysms. Mycotic aneurysms of the abdominal aorta are very rare and none were encountered in the present series. It is probable that in the future they will be even rarer because of the widespread use of antibiotics. Mitchell and Clairveaux[12] reported a case with rupture of a mycotic aneurysm of the abdominal aorta following pneumococcus endocarditis and they list five cases from the literature which were secondary to bacterial endocarditis. The youngest patient on record to our knowledge was a child 7 years and 9 months old, reported by Baginsky in 1908.[13] This patient had a streptococcal endocarditis and an aneurysm of a subclavian artery as well as the abdominal aorta.

Wilcox and Fisher[14] described a case of particular interest. A 54 year old woman developed subacute bacterial endocarditis (*Streptococcus viridans*). Emboli occluded the femoral arteries of both legs. Following heavy penicillin therapy her temperature returned to normal, clubbing of her fingers disappeared and the spleen was no longer palpable. The patient nevertheless did not feel well. She had pains in the legs, hips and lower abdomen and a persistent pulse, about 120 per minute. The blood cultures were persistently negative. Thirty-four days after she became afebrile, a pulsatile mass appeared below the umbilicus. Twenty days later she died of a rupture of this aneurysm in a matter

of minutes. At autopsy, bacteria were found in the wall of the aneurysm, but none could be found in the blood or the heart valves.

Rupture of Aneurysms of the Abdominal Aorta. Rupture is the most dreaded terminal event in the history of these aneurysms. Seventeen aneurysms in the present series ruptured. In nine of these, the aneurysm had been diagnosed before the rupture in periods ranging from several months to two years. In seven patients the diagnosis of aneurysm was made only when it ruptured. In none of these cases was an increase in the size of the mass noted before it ruptured. In one case, however, there was a sudden appearance of a nonpulsating mass on the day of the rupture. All 17 of these patients died as a result of the rupture. This has been the usual experience. However, with the advent of newer surgical technics, we should re-examine the possibilities of this complication. Logically, the best method is prevention by excision and replacement of the aneurysmal segment prior to the rupture. Even symptomless aneurysms may rupture, so that they do not guarantee safety; but frequently the patient is not seen until the aortic wall is perforating and rupture is imminent or taking place. It is common belief that it is then too late to operate, but from now on it appears that, in the best of surgical hands, an increasing number will be successfully operated upon.

The series reported by Goldowsky[11] is of interest in this regard. He reported 15 cases of spontaneous, abdominal aortic perforation verified by postmortem examinations. He emphasized that, contrary to common belief, rupture of the abdominal aorta is not a cause of sudden death. The patients in his series survived from 5 hours to 27 days. Twelve patients survived more than 24 hours, 8 patients more than 5 days. It appears, therefore, that in each patient in this entire series there was *time* for surgical intervention. In our series, the survival period was shorter, being from 1 to 3 days, but in some there was ample time for surgical intervention. Time is only one factor but has been generally thought to be too brief for such an approach. Goldowsky's cases were reported in 1952, and most of them died prior to the era of aortic grafts; but they are instructive. In 10 patients, the aneurysms were below the renal arteries and therefore might have been considered amenable to surgery. Arteriosclerosis was marked and thought to be the etiologic factor in each case. No syphilis was found. This was in contrast to the findings of Nixon,[15] who in 1911 reviewed the literature and found 223 cases of abdominal aneurysms of which 152 ruptured. He reported that the "majority" had syphilis. As pointed out above, however, that does not prove that syphilis was an etiologic factor in these aneurysms, unless proved pathologically in each case. DeBakey[16] has made notable strides in surgery for ruptured aneurysms, having been able to operate successfully on 73 per cent of his cases.

Type of Aneurysm. In 58 cases the type of aneurysm was satisfactorily classified at autopsy or laparotomy. In 32 patients, the aneurysm was fusiform in type. In 26 patients, the aneurysm was saccular. This was a high percentage of saccular abdominal aortic aneurysms, compared with most series. Dissecting aneurysms usually start in the thoracic area and the dissection proceeds distally into the abdominal area. It may also dissect toward the heart. Dissecting aneurysms were not included in this study, except for a single one that was confined to the abdominal aorta.

Treatment. A total of 85 of these patients received no specific treatment for their aneurysm. This reflects the fact that most of them were seen in an era when surgical treatment was not available. Figure 4 shows the increase in interest in the surgical approach in the past four years, as indicated by the request for grafts from the Blood Vessel Bank.

The Surgical Approach. If surgery is to be elected it must be justified by evidence that the risk is less than the prognosis without surgery.

Fifteen of these patients had resection and graft. Nine of these were successful. Failures were due to rupture of the anastomosis in 2 cases, uremia in 2 cases, leakage of the aneurysm in 1 case, and rupture preoperatively in 1 case. Four cases were wrapped with plastic material. The results were successful in three cases. One died, 1 day postoperatively, of pulmonary edema and shock.

Two patients were treated by the Blakemore

wiring procedure with the following results: 1 patient is still alive after 5 years, 1 died 3 days postoperatively and 1 patient had his aorta ligated below the renal arteries, but developed gangrene of the legs and died.

In Dr. Jere Lord's series subjected to surgery, 11 were resected and grafted, of which 5 have been successful; 5 were treated by wrapping, of whom 2 are alive (1 month and three and one-half years postoperatively). Two were injected with sodium dicetylphosphate, one is alive.

Dr. S. W. Moore has operated on 11 patients for abdominal aortic aneurysm and 9 have been successful, with satisfactory postoperative courses up to two years. One patient died in the hospital. He had a history of two myocardial

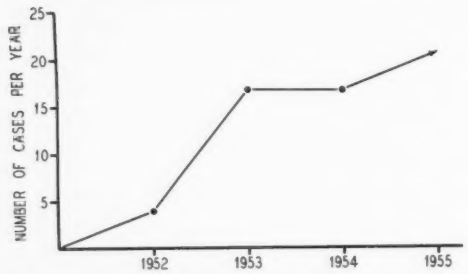

FIG. 4. Illustrates the increase in the number of homologous grafts used to replace abdominal aortic aneurysms from the New York Blood Vessel Bank (courtesy of Dr. A. A. Lazzarini).

infarctions. He was operated on for a ruptured abdominal aneurysm and after this died of thrombosis of the left common iliac artery with rupture. The other death occurred 5 weeks after operation from an infection of the anastomosis of the right common iliac artery with rupture and hemorrhage. One living patient is seriously ill with heart failure.

In recent years this problem has been vigorously attacked by numerous surgeons of note. The introduction of fine wire into the aneurysmal sac to encourage reinforced clot formation with electric stimulation was developed and studied with great care by Blakemore and his co-workers. The wrapping of the outer walls of aneurysms by cellophane and other fibroplastic-stimulating materials has been carried out by numerous surgeons. While the results in certain specific patients have apparently been encouraging, many of them have died at the time of operation or soon after, so that the proof that the prognosis is on the average better for the patient is difficult to establish and in our opinion lacking. The over-all operative mortality in Blakemore's series of 1954 was 37.2 per cent. Of these, rupture was the cause in 19.1 per cent (20 cases). Nine of these showed evidence of rupture before operation, 3 ruptured at operation and 8 ruptured postoperatively; 18.1 per cent died of other causes, including heart failure and thrombosis. If wrapping is attempted, Blackmore prefers to use a strong plastic cloth such as Nylon or Vinyon N.

TYPES OF OPERATION

1. Aortic occlusions proximal to aneurysm (no longer used).
2. Thrombo-endaortarectomy and wrapping (no longer used).
3. The production of thrombosis within the aneurysm by means of wiring, with or without endothermy (no longer used).
4. Partial or complete external reinforcement or wrapping (used by some surgeons when graft is not feasible because of patient's condition or technical difficulty).
5. Resection and replacement (favored today).
   a. Homograft.
   b. Prosthesis of Dacron, Orlon, Vinyon N or other plastic (in the developmental phase).

Not all of the patients who have had the wiring procedure have done poorly. For example, patient R.H., age 77, was operated on in 1950 for an abdominal aneurysm, at which time silver wire was introduced. In 1951 a second operation was performed and more silver wire inserted. Both operations were performed by Dr. Blakemore. In 1955 the patient was alive and active and was admitted to The New York Hospital for a ureteral calculus, which was passed. Incidentally, he has also survived a myocardial infarction, with development of atrial fibrillation, left bundle branch block and periodic cardiac decompensation.

While a few surgeons still use wrapping in some cases where resection seems impractica

the interest today is definitely in the direction of resection of the aneurysm, with the substitution of a graft of either homologous aorta or a prosthesis of plastic material such as Vinyon N or Orlon. This type of procedure is still fraught with considerable risk but the great progress of the past five years indicates more successful use in the future. Saccular aneurysms are frequently attached by a pedicle that may permit lateral clamping and suture. This procedure often produces excellent results and has been reported by many surgeons including Dubost and Dubost,[17] Bahnson[18] and DeBakey, Cooley and Creech.[16, 19] The sac should be removed, if possible. If a whole sac is left in place, the danger of infection is considerable. If a portion of the sac is adherent to a vital area such as the inferior vena cava, it may be necessary to leave it in place. This has been successful in many cases.

So far as we can determine, the first successful homologous graft to replace a fusiform aneurysm of a human aorta was performed by Dubost on March 29, 1951.[20] The graft was functioning and in good condition when reported three years later.[17] This was a graft of considerable size, extending from the level of the renal arteries to include the upper portion of the right common iliac artery and was attached to the left common iliac artery. Dubost and Dubost[17] emphasized that the aorta near an aneurysm is often thickened, friable and indurated with calcareous patches or medial necrosis. It is, therefore, easily cut by sutures, producing secondary ruptures. They mentioned ruptures that occurred on the twenty-ninth day and six months after resection. They also point out that if syphilis is present, antibiotic treatment should certainly be given prior to surgery. While we must agree to this, the effect on the outcome of any specific operation may be doubtful, especially in the case of abdominal aneurysms, which are so rarely syphilitic today.

The number of homografts performed since that of Dubost cannot be determined because they are now being undertaken in many areas of the world today. The degree of over-all success is also difficult to determine; but on the basis of our knowledge from wide travel and work in various countries, it can be stated that to this date there is a great variation in the results. This is to be expected with any new, highly technical procedure and is based on lack of experience with this operation, unsatisfactory preparation and preservation of the grafts and lack of criteria of indications and contraindications for this type of procedure, as well as all the usual problems of surgery in the elderly patient with widespread atherosclerosis and, frequently, other diseases. Outstanding reports have come from the clinics of Bahnson[18] and DeBakey.[16, 19] In 1954, Bahnson[18] reported 14 patients in whom he had performed aortic homografts and 11 were alive and well (1 patient required amputation of a leg). In 1955, DeBakey and his associates reported that 49 abdominal aneurysms had been resected and grafted. Of those who recovered, 36 were reported to be in excellent condition, while none were in poor condition. Thirteen died, 7 of coronary disease, 4 died early of renal failure, 2 died later of unspecified causes. In all but six cases the aneurysm involved the bifurcation, which had to be resected. The death rate of the operation was 16 per cent below 60 years of age and 32 per cent above 60 years of age. In 13 patients, Orlon-cloth prostheses had been used to replace aortic bifurcations with satisfactory results. DeBakey presented additional figures before the Annual Session of the American Heart Association in October 1955 (table 10).

One of the technical steps of major concern has been the prolonged occlusion of the aorta with the secondary ischemia of the tissues of the legs. We have observed several examples of failure of adequate restoration of circulation after this procedure with loss of one or both legs. This has occurred in patients who had

TABLE 10.—*Operative Results (DeBakey)*

Total operations		Mortality
Nonruptured cases	142	10%
Ruptured cases	22	40%
Recent figures—Mortality		
Nonruptured cases	5 out of 71 cases (7%)	
Ruptured cases	4 out of 11 cases (36%)	

demonstrated marked evidence of occlusive arteriosclerotic disease prior to operation. Therefore, proper account of this risk should be undertaken in the preoperative study of the patient. DeBakey and Cooley state that for aneurysms below the renal arteries, arrest of circulation with an aortic clamp for 120 minutes has not produced residual ischemic changes. They have used two procedures to reduce this risk: (1) lumbar sympathectomy as part of their operation and (2) injection of 10 mg. of heparin into the aneurysm, just before occluding the aorta, to retard thrombophilic effects of retarded blood flow in the distal vascular bed. It is our belief that this dosage is probably on the low side for this purpose, but we recognize the undesirability of producing too generalized a bleeding tendency during such an operation. They claim that most patients actually had improved circulation to their lower extremities after the operation. These results certainly justify much wider use of this technic by properly equipped surgical teams.

For successful, widespread use of homografts, a highly efficient Blood Vessel Bank with a large source of suitable grafts is a requisite. This paper does not attempt to discuss the technic or functioning of such a bank. It appears that the demand may well outstrip the supply, even in large cities, especially since in many cases bifurcations are needed. In smaller communities and for emergencies, prostheses of synthetic material should be available, if practical. Their use has been explored by numerous workers, notably Blakemore[1] and DeBakey.[16] Blakemore has used 37 denier, 144 by 90 strands per square inch of Vinyon N cloth. In dogs sacrificed 19 to 153 days postoperatively, he found all prostheses to be encased in fibrous tissue 1 to 5 mm. in thickness. The inner surface was covered with a thin, translucent film, consistent with multiple layers of flattened cells and collagen fibers with fibroblasts growing through the interstices of the cloth. Of the first four cases in man, using this material, 1 died in 5 days from uremia and 1 died of hemorrhage from rupture of a thinned posterior wall proximal to the line of suture. Two patients did well and were discharged with good pulsations in the arteries of the feet. As mentioned above, DeBakey reported 13 such cases, using Orlon and Nylon, with good results. While at present homografts are favored, the use of such prostheses should be developed. They offer the great practical advantages of ease of preparation and preservation, and they can be woven or cut to fit almost any foreseeable demand in terms of vessel length or arrangement. Careful preoperative studies make a satisfactory analysis possible in most cases. However, the decision whether or not to attempt a surgical procedure has sometimes been difficult without laparotomy.

E.M., a 54 year old man, a patient of Dr. Edward Keefer, exemplifies this point. Six months prior to admission he developed a watery diarrhea that lasted two weeks. There was no bleeding. Following this, he noticed a sharp, aching left abdominal pain. There were occasional episodes of nausea and vomiting. There was a 12 pound weight loss believed to be related to diminished intake.

On physical examination a firm, pulsating mass, measuring 4 by 3.5 cm., could be felt in the left upper quadrant, just to the left of the umbilicus. Systolic and diastolic murmurs could be heard.

Roentgenographic studies showed the calcific outlines of an abdominal aortic aneurysm. Intravenous pyelograms showed a nonfunctioning left kidney, the outline of which could not be clearly seen.

An aortogram revealed a somewhat enlarged thoracic aorta, an abdominal aneurysm extending from just below the origin of the superior mesenteric artery, and partially involving this area and the celiac axis, to below the bifurcation of the aorta. The left renal artery was apparently occluded in the wall of the aneurysm, and the left kidney was nonfunctioning. The right renal artery was not visualized and arose also from the aneurysm wall. There was, however, excellent visualization of a right double kidney. The aneurysmal sac consisted mainly of a large clot with a relatively narrow central channel. It was concluded by Dr. Keefer

hat this aneurysm was inoperable in every espect.

The symptoms were progressive, and the patient was later explored in the hope that something might be accomplished to help him; but his was not possible. He was alive two years ater. He had gained 40 pounds and had no omplaints but the large pulsating mass. This xemplifies the difficulties of prognostication, ince his condition has continued to be unexpectedly good.

Another patient of Dr. Keefer's is of interest because of the very long operative procedure.

J.P., male, age 65, considered himself in good health until three weeks prior to admission, at which time he noted a mild, crampy abdominal pain located about the umbilicus. It increased over a 12 hour period and was associated with anorexia followed by sudden unconsciousness lasting about 10 minutes. After this episode he suffered mild, intermittent, crampy abdominal pain. The patient denied syphilis and had noted no coldness, paresthesias or claudication pains in the legs. He had not been aware of an abdominal mass, pulsations or back pain.

Physical examination revealed a firm, pulsating mass to the left of the midline, measuring 10 by 14 cm., and extending from the epigastrium to the level of the iliac spine. The femoral, dorsalis pedis and posterior tibial pulses were felt.

An abdominal aortogram revealed a large aneurysmal dilatation of the abdominal aorta with associated soft tissue mass, which undoubtedly represented laminated clot.

Course. Six days after admission, a resection of the abdominal aorta was carried out by Dr. Edward Keefer because of a large, ruptured aortic aneurysm. A homologous arterial graft was inserted below the renal arteries and including the aortic bifurcation (figs. 5 to 8). The patient was on the table thirteen and one-half hours. He received 8,650 ml. of whole blood. He had a rather stormy postoperative course but gradually improved. His dorsalis pedis and posterior tibial arteries continued to be patent. On the twenty-eighth postoperative day he was discharged from the hospital without pain. His

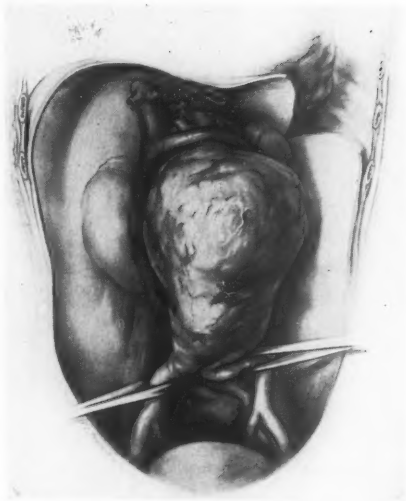

FIG. 5. Preoperative appearance of aneurysm of patient J. P. (courtesy of Dr. Edward Keefer).

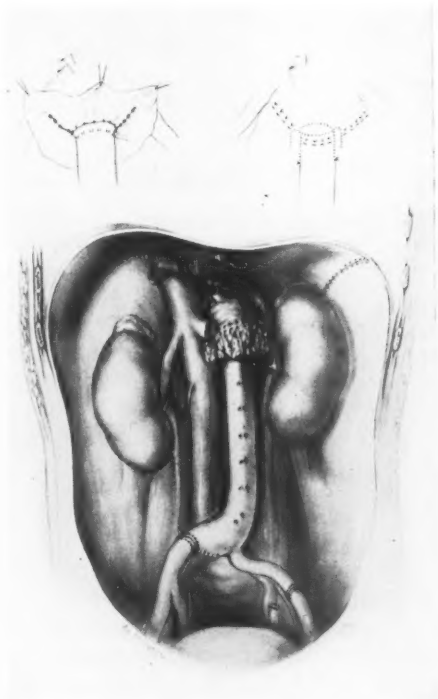

FIG. 6. Replacement of aneurysm by extensive graft, patient J. P. (courtesy of Dr. Edward Keefer.)

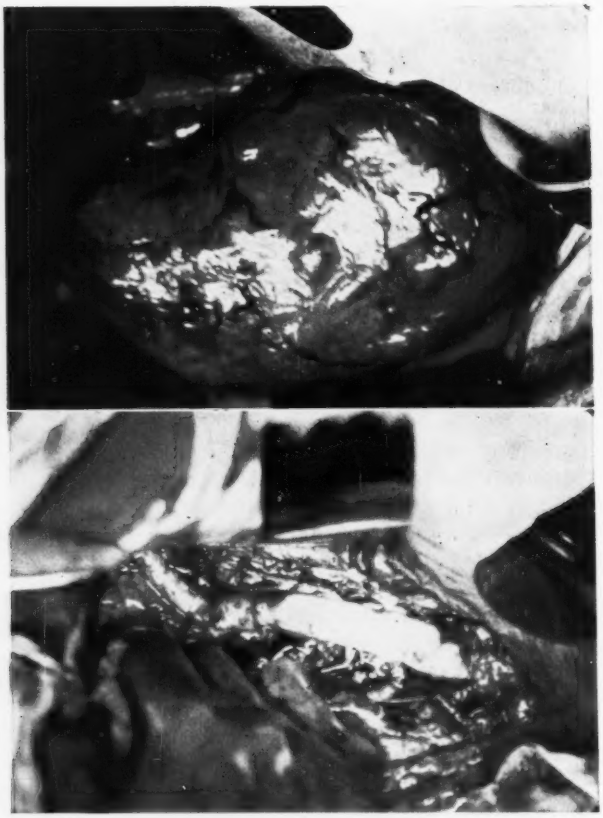

FIG. 7. Large abdominal aneurysm in situ (courtesy of Dr. Edward Keefer).
FIG. 8. A homologous aortic graft that has replaced an abdominal aortic aneurysm (courtesy of Dr. Edward Keefer).

only complaint was minimal weakness after being up and about for considerable periods. He is still alive two years later and doing well.

Postoperative Care. Our observations and review of such cases lead us to believe that in some instances the technical surgery has been excellent, but a leg or a life has been lost because of lack of attention to certain details during the postoperative period. We therefore suggest that particular attention be paid to the following:

1. In most patients the feet should be 6 inches below the heart level to encourage return of good arterial circulation. On many surgical services, a common procedure is to elevate the foot of the bed and thought is not given to the physiologic needs after this procedure.

2. Prophylactically, heparin should be instilled into the aneurysm or the distal iliac arteries when the proximal artery is occluded to minimize the risk of sludge or thrombus formation.

3. If there is evidence that the circulation is poor, this may well be due to sludge or soft-clot formation. Heparin should be started immediately. It should preferably be given into the femoral arteries by continuous drip or in daily amounts of 300 mg. per 1,000 ml. of 5 per cent dextrose. This will encourage disintegration of the sludge or clot rather than consolidation of it and may well save an extremity. This may be continued for 8 to 10 days or an oral anticoagulant may be substituted after th

st 3 to 4 days. The use of anticoagulants is t universal for this purpose but appears to increasingly accepted.

4. Peripheral vasoconstricting drugs should avoided unless vitally needed to keep the od pressure up. They may further endanger tremities already in jeopardy from poor culation.

5. Unless there is an overbalancing contra- dication, fluids must be administered at a gh level of 2,500 ml. or more a day, since hydration encourages thrombosis.

6. The electrolyte balance should be con- olled carefully.

7. Antibiotic therapy should be administered ophylactically.

8. Gastric suction should be used freely to prevent distention, paralytic ileus and pressure on the new graft site.

9. Active exercise of the lower extremities should begin with the return of consciousness.

10. The use of an oscillating bed is justified, especially if the circulation of the legs is impaired.

Indications for Resection and Graft for Abdominal Aortic Aneurysms. There are some justifiable differences of opinion regarding the indications and contraindications for this type of surgery. There are surgeons who believe that any aortic aneurysm should be operated upon, regardless of level or type. Others feel that if the aneurysm is above the renal arteries or involves the renal arteries the results will not justify the surgery. Our present indications for operation are as follows:

(1) A patient who has an abdominal aortic aneurysm and whose general condition seems good enough to tolerate surgery of this magnitude;

(2) a palpable pulsating mass in or near the midline of the abdomen (a mass increasing in size under observation makes the operation urgent);

(3) pain in this area, intermittent or persistent, especially if severe enough to require narcotics;

(4) evidence of rupture or leakage constitutes an emergency indication for operation;

(5) anteroposterior and lateral x-ray films, showing the calcific outline of an aneurysm;

(6) an aortogram, demonstrating an aneurysm that appears operable;

(7) availability of a suitable graft or prosthesis;

(8) a surgical team with sound experience with this type of surgery;

(9) the indications are the same regardless of the etiology of the aneurysm, although the outlook for syphilitic aneurysms (fortunately rare) is poorer than for the other types.

Indications for Great Caution or Operation Only Under Unusual Circumstances

(1) Recent or repeated myocardial infarction;

(2) definite evidence of coronary insufficiency, (some surgeons suggest the simple operation of wrapping the aneurysm, if progression forces an operation in the face of either of these two contraindications);

(3) extreme hypertension, e.g., 240/140 mm. Hg, which should be reduced prior to operation, if possible;

(4) marked arterial insufficiency of the lower extremities with risk of, or impending, gangrene;

(5) involvement of the renal arteries with renal insufficiency.

Absolute Contraindication. The presence of another disease that will inevitably kill the patient within a short time.

Results of Surgery. The immediate results appear to justify the surgical approach, when the criteria outlined above are utilized. The results appear to maintain a favorable balance throughout a two year follow-up period. There are an insufficient number of patients who have been followed for a longer period to make final conclusions possible regarding a long-range comparison with untreated cases.

Conclusions

1. Technical advances in the surgical treatment of abdominal aortic aneurysm justify further examination of this approach.

2. The great majority of abdominal aortic aneurysms are arteriosclerotic; syphilitic and mycotic aneurysms are now very rare.

3. The life expectancy is poor, with 85 to 95 per cent of the patients dying within 5 years of the diagnosis. This type of aneurysm should be regarded as seriously as cancer.

4. The symptoms and signs are varied and often masked by other pathologic processes but their careful analysis frequently leads to the correct diagnosis.

5. Roentgenographic studies, both with standard technics and visualization with contrast media, are usually helpful in confirming the diagnosis.

6. Each case should be analyzed in terms of suitability for surgery, and the great majority can be successfully operated upon.

7. Various types of surgical approach have been tried, but today the emphasis is on resection of the aneurysm and its replacement by a graft.

8. Homologous aortic grafts are more widely used at present, but plastic grafts of Nylon, Orlon, and Vinyon are being tried and will possibly be used in the majority of cases in the future.

9. The indications, reasons for caution and contraindications have been analyzed.

10. Rupture of an abdominal aneurysm is the most common fatal complication, but with modern technic and prompt action, an increasing number of these cases are being successfully operated upon.

11. The technical advances of surgery have greatly improved the outlook for the treatment of the aneurysm itself, but it must be borne in mind that most of these patients are over 60 years of age and have widespread vascular disease or other malignant disease from which more than 50 per cent of them will die within five years.

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ABSTRACTS

BACTERIAL ENDOCARDITIS

Hall, W. H., and Gold, D.: Shock Associated with Bacteremia. Arch. Int. Med. **96:** 403 (Sept.), 1955.

The authors reported on 35 patients with associated bacteremia and shock. The mortality rate was 51 per cent. Typical signs of shock were present at the onset of the hypotension in 15 of 26 patients. In the remainder, hypotension was masked by flushing of the skin, bounding pulse, and other circulatory changes caused by the infection. Shock appeared late in these patients.

Prompt use of effective antibiotics controlled the bacteremia, but shock frequently remained unchanged and often led to death. Blood and plasma transfusions frequently raised the blood pressure level somewhat, but did not reduce the fatality rate. Vasoconstrictor drugs in large doses were very useful in restoring the blood pressure: levarterenol and metaraminol were the most effective. Steroid hormones did not lessen the shock. Shock and death were not caused by adrenal insufficiency. Of the 14 patients studied at necropsy, 7 showed signs of cardiac disease that may have contributed to the fatal outcome. Widespread damage to small blood vessels and petechiae were often found.

BERNSTEIN

Hamburger, M., and Carleton, J.: The Similarity of Bactericidal Rates of Penicillin for Streptococcus Viridans from Successfully Treated Cases of Bacterial Endocarditis and from Cases Which Relapsed. J. Lab. & Clin. Med. **46:** 41 (July), 1955.

Ten to 15 per cent of cases of penicillin-treated, subacute bacterial endocarditis caused by streptococcus viridans relapse, despite the proved, continuing sensitivity of the organisms to the antibiotic. The rate of bactericidal action of penicillin and the number of days required to sterilize cultures were determined in a series of 5 strains of penicillin-sensitive *Streptococcus viridans* recovered from successfully treated patients with bacterial endocarditis, and 5 strains from 3 patients who relapsed following similar treatment.

The rate of bactericidal action and the time required to sterilize broth cultures were practically the same for the strains from both groups of patients, even with 3 different concentrations of penicillin. However, the number of bacteria inoculated proved to be an important variable. The density of bacterial population was more important in determining the sterilization time of these cultures than the source of the culture or the concentration of penicillin, provided the latter exceeded the minimal inhibiting concentration.

It may be assumed, therefore, that the relapses in the 3 patients were not due to any characteristic of the streptococci themselves, but rather to a failure to achieve and to maintain an adequate bactericidal concentration of penicillin within the vegetation.

CORTELL

Beeson, P. B.: Subacute Bacterial Endocarditis: Optimal Duration of Treatment. (editorial). Am. J. Med. **19:** 1 (July), 1955.

Extensive experience with antibiotic therapy of subacute bacterial endocarditis, has established that (1) penicillin is usually much more effective than other antibiotics, (2) moderately large doses should be given and (3) the period of chemotherapy must be of some length. Evidence indicates that antibiotic therapy can be safely terminated after 2 to 4 weeks in properly selected cases. Two principal criteria for such selection would be short duration of illness and an infecting organism sensitive to

penicillin. A further indication would be prompt clinical improvement after the inception of antibiotic treatment. Conversely, prolonged treatment is advisable with (1) long duration of illness before beginning of therapy, (2) an infecting organism relatively insensitive to penicillin, and (3) patients without demonstrable bacteremia in whom diagnosis may be delayed. The physician must maintain a close follow-up for evidence of relapse, particularly during the first month or two. A relapse, while undesirable, is not necessarily disastrous, as retreatment may yet be successful. In a disease of such gravity, conservatism is proper. Any error should be in the direction of overly long treatment.

HARRIS

Parkhurst, G. F., and Decker, J. P.: Bacterial Aortitis and Mycotic Aneurysm of the Aorta: A Report of Twelve Cases. Am. J. Path. **31:** 821 (Sept.–Oct.), 1955.

Twelve cases of bacterial infection of the wall of the aorta were presented. Associated mycotic aneurysm formation was observed in nine of these. The lesions were all in the thoracic aorta. Microscopically, underlying aortic disease (atherosclerosis, cystic medionecrosis and congenital hypoplasia) was found in 9 cases. In 4 cases the source of infection was bacterial endocarditis, in 3, pneumonia or mediastinitis and in 5, the source was a remote infection, such as cellulitis or gonococcal urethritis.

HARVEY

Hall, B., Dowling, H. F., and Kellow, W.: Successful Short-Term Therapy of Streptococcal Endocarditis with Penicillin and Streptomycin. Am. J. M. Sc. **230:** 73 (July), 1955.

Subacute bacterial endocarditis caused by penicillin-sensitive alpha and gamma streptococci, was treated in 15 patients with combined penicillin and streptomycin therapy. The respective doses of these drugs were from 20,000,000 to 74,000,000 units and from 15 to 34 Gm. The duration of therapy varied from 10 to 17 days. Of the entire group, 2 patients died during treatment, and 1 remained febrile until treated for a period of 6 weeks with larger doses of penicillin alone; the remaining 12 patients (80 per cent) recovered from the disease, following the short-term course of combined antibiotic therapy. The experience reported here indicates that penicillin in doses of 600,000 units of aqueous procaine penicillin G, at 6 hour intervals, intramuscularly, for 10 days and 0.5 Gm. of a mixture of streptomycin and dihydrostreptomycin, intramuscularly, at 6-hour intervals for 5 days, and at 12-hour intervals for an additional 5 days, is an effective method of treatment for cases in which the streptococcus organism is sensitive to 0.2 units of penicillin, or less, per ml. The sensitivity of the organism to streptomycin is not indicative of the response to be expected with combined therapy, since equally good results were observed where the organism was susceptible to 32 mcg. of streptomycin per ml., as where 0.2 μg. caused inhibition.

SHUMAN

Geraci, J. E.: Further Experiences with Short-Term (two weeks) Combined Penicillin-Streptomycin Therapy for Bacterial Endocarditis Caused by Penicillin-Sensitive Streptococci. Proc. Staff Meet., Mayo Clin. **30:** 192 (May), 1955.

Twenty-three additional, consecutive patients with bacterial endocarditis caused by penicillin-sensitive streptococci have received short-term (2 weeks) combined penicillin and streptomycin-dihydrostreptomycin therapy. One million units of aqueous procaine penicillin and 1 Gm. of combined streptomycin-dihydrostreptomycin (0.5 Gm. of each) administered intramuscularly every 12 hours gave uniformly good results. No failures in treatment or relapses occurred in 20 living patients. Three patients died of complications of their valvular infection.

Altogether, 46 patients were treated with short-term combined therapy with no failures of treatment or relapse in the living patients. This form of therapy for endocarditis caused by penicillin-sensitive streptococci should be considered conventional. A plea is made for increased awareness of the occurrence of bacterial endocarditis, earlier diagnosis and earlier treatment, so that fewer patients will die of complications from valvular infection.

SIMON

CONGENITAL ANOMALIES

Cooley, D. A.: Surgical Closure of Atrial Septal Defects. Surg., Gynec. & Obst. **100:** 268 (March), 1955.

Atrial septal defects are among the commonest congenital cardiac anomalies. The prognosis is relatively good, the average duration of life being 40 years. In some patients the condition is incapacitating, however, with attacks of pneumonia, pulmonary infections, cardiac arrhythmias, or decompensation complicating the clinical course.

The author describes a method of surgical closure of an atrial septal defect. This consists first of inserting a finger into the right atrium for the purpose of exploring the lesion and determining the location of the openings of the various vessels opening into the atria. Then the exploring finger is withdrawn, and under palpatory guidance, effective closure of the septal defect is carried out by transatrial insertion of a septal purse-string suture. This operation was performed on three patients with successful outcome.

ABRAMSON

Cooley, D. A.: Surgical Closure of Ventricular Septal Defects; Preliminary Report of New

Technique. Surg., Gynec. & Obst. **101:** 153 (Aug.), 1955.

The author discusses the altered hemodynamics associated with ventricular septal defects and points out that the ones located in the membranous septum tend to remain patent throughout the cardiac cycle. On the other hand, those lower down constrict during systole, thus reducing the volume of the shunt. The defects vary in diameter from 0.2 to 3 cm. The ones that are less than 1.5 centimeters in diameter usually cause few, if any, symptoms, whereas the larger ones generally produce significant cardiac disability. Since congenital interventricular defects seldom heal spontaneously, the problem of surgical closure requires investigation.

The author describes a method of treatment of ventricular septal defects involving a modification of the technic of atrial septal suturing. The procedure consists of passing mattress sutures through the upper third of the ventricular septum to close the opening in the membranous portion. Accurate placement of the sutures avoids interference with blood flow into the pulmonary artery and aorta, disturbance in function of the cardiac valves and obstruction to coronary arterial supply to the myocardium. The operation was performed on 2 patients, both of whom survived the procedure and showed early evidence of improvement.

ABRAMSON

Callahan, J. A., Brandenburg, R. O., and Swan, H. J. C.: Pulmonary Stenosis and Interatrial Communication with Cyanosis. Am. J. Med. **19:** 189 (Aug.), 1955.

Clinical and hemodynamic data are presented in 10 cases of pulmonary stenosis and interatrial communication with cyanosis, a condition probably next in frequency to tetralogy of Fallot among cases of cyanotic congenital heart disease with polycythemia and clubbing. Cyanosis was present in 8 cases at birth or in infancy and probably began in infancy in another. In the remaining patient, transient cyanotic episodes were noted in infancy and became persistent at 7 years of age. Three patients had combined valvular and infundibular stenosis; 6 had valvular stenosis only; 1 had infundibular stenosis only. One patient had a right-sided aortic arch, which is rare in this syndrome. Considerable variation was noted in roentgenograms of the chest. The shadow of the pulmonary artery was visualized in 8 of the 10 patients on routine anteroposterior roentgenograms and was prominent in 5 patients. Systemic blood flow was greater than pulmonary flow in each case. In 5 patients the right-to-left shunt was 50 per cent or more of systemic flow. The technic of selective injections of T-1824 was of great value in demonstrating and localizing the site of the right-to-left shunts in the absence of any shunt from left to right.

The cardiac malformations of pulmonary stenosis and interatrial communications are potentially curable at present. Because such corrective surgery is available, many authorities have urged that these patients be treated by pulmonary valvulotomy and not by a shunt operation. Nine patients reported in this series underwent pulmonary valvulotomy. Two patients died postoperatively, a third of intractable bleeding, 48 hours after operation. The remaining 6 patients improved but a residual right-to-left shunt was probably present in all cases.

HARRIS

Foster, W. D.: Congenital Fibro-elastosis of the Endocardium with Unusual Associations: A Report of Two Cases. J. Path. & Bact. **69:** 331 (Jan.–Apr.), 1955.

The author reports on two cases of fibroelastosis, one in an infant of 3 months and another in an infant 2 days old. In one, the left coronary artery arose from the pulmonary artery. The role of anoxia is discussed as a possible etiologic factor in the production of fibroelastosis. Calcification of the myocardium was present in the second case. It was thought to be of little significance—a natural occurrence in a vascular fibrous tissue.

HARVEY

McCue, C. M., Henningar, G. R., Davis, E., and Ray, J.: Congenital Subaortic Stenosis Caused by Fibroma of Left Ventricle. Pediatrics **16:** 372 (Sept.), 1955.

A case is presented in which a primary tumor of fibroblastic histogenesis, arising in the intraventricular septum, produced the clinical picture of subaortic stenosis. A 4-year-old child with a basal systolic murmur and thrill, moderate aortic second sound and an electrocardiographic pattern of left ventricular strain, was followed from the age of 2 months. Growth was normal, and exercise tolerance was always good. The autopsy findings are also presented.

HARVEY

Aubry, J.: Three Anatomic Clinical Observations of Congenital Low Aorticopulmonic Communications. Arch. mal. coeur **48:** 685 (July), 1955.

Three anatomically proved cases of a congenital, low fistula between the aorta and pulmonary artery are described. In two, a complete clinical study including angiocardiography and cardiac catheterization was possible. The principal diagnostic elements distinguishing such a condition from a patent ductus are a systolic murmur (in 50 per cent of the cases) in the fourth to sixth left intercostal space, a positive ether test, pulmonary hypertension, passage of the catheter directly into the aorta, equal arterial saturation in all four extremities, and early opacification of the aorta and of the right subclavian artery at angiocardiography.

In two of these cases, an attempt was made at

surgical repair of the lesion, with fatal outcome. Despite occasional reports of successful closure of the fistula, the author believes that at present the operation is hazardous and should not be encouraged.

PICK

Giraud, G., Chaptal, J., Latour, H., Puech, P., and Jean, R.: Congenital Aortico-pulmonic Communication. Its Diagnosis by Catheterization of the Aorta across the Communication. Arch. mal. coeur **48:** 567 (June), 1955.

A case is described wherein the diagnosis of a large, aortic-pulmonary fistula with a crossed shunt, was made clinically on the basis of physical and laboratory findings. The authors present suggestive, probable, and definite criteria to differentiate this condition from other congenital anomalies, in particular from a patent ductus.

Clinically, the condition should be suspected when equal cyanosis is present in all 4 extremities; a superficial continuous murmur with a feeble diastolic component is heard over the third intercostal space, and both aorta and pulmonary artery show marked expansible pulsations at fluoroscopy. Probable hemodynamic criteria are symmetrical arterial desaturation in all 4 extremities, at rest and after exercise, and a positive ether test on injection above the pulmonary valves. Conclusive criteria are vizualization of the site of the fistula by retrograde aortography and passage of a catheter into the aorta across the communication, a procedure which also permits approximate estimation of the size of the opening between the 2 vessels.

PICK

Lenégre, J., Cattoir, E. and Gerbaux, A.: Contribution to the Study of Ebstein's Disease. Arch. mal. coeur **48:** 632 (July), 1955.

Four new observations are reported of Ebstein's disease, 2 proved by autopsy and 2 diagnosed by cardiac catheterization. One of the proved cases, a 65 year old man, presented the clinical picture of cirrhosis and tricuspid insufficiency.

According to the authors, the diagnosis of Ebstein's anomaly during life is possible by correlating clinical, radiologic, electrocardiographic and hemodynamic findings. Cyanosis and clubbing are present, though to a varying degree, and in most of the cases are due to the associated atrial septal defect. A systolic and sometimes a faint diastolic murmur are heard over the midprecordium, and triple or quadruple rhythm of the sounds is not uncommon. The heart is enlarged and of globular shape, while the pulmonary fields are translucent due to hypovascularity. The electrocardiogram shows right bundle branch block and frequently large P waves. The outstanding angiocardiographic features are enormous dilatation of the right atrium and slow filling of the right ventricle and pulmonary arteries. At catheterization the right ventricular pressure is normal or low, and the pressure gradient between right atrium and ventricles is minimal. On the basis of these findings, the important differential diagnosis from tetralogy of Fallot and trilogy can be made. Surgery is not indicated and is dangerous in Ebstein's disease.

PICK

Lezuime, J., and Denolin, H.: Notes Concerning Circulatory Dynamics in the Course of Persistent Ductus Arteriosus. Acta cardiol. **10:** 363 (Fasc. 4), 1955.

Hemodynamic and electrocardiographic data in 17 cases of patent ductus arteriosus were reviewed with particular reference to pulmonary hypertension. In 15 cases the pulmonary pressure was normal or practically so. The pulmonary hypertension in the two remaining cases was thought to be congenital and the result of persistence of a fetal type of pulmonary circulation. Such a pressure elevation modifies the usual clinical picture of the disease in that the patients are incapacitated, the heart is enlarged and the murmur is only systolic. Exercise leads to arterial desaturation attributable to a transient reversal of the A-V shunt or to exaggeration of a pre-existent V-A shunt. To explain the greater frequency of pulmonary hypertension reported in the Mexican literature, the authors invoke anoxia existing at high altitudes, which favors persistence of a fetal-pulmonary circulation.

There are no electrocardiographic findings characteristic of a patent ductus arteriosus. In the present study it was not possible to establish a precise correlation between hemodynamic and electrocardiographic alterations.

PICK

CORONARY ARTERY DISEASE

Meesman, W., and Schmier, J.: Cardiac Failure Secondary to Critically Severe Coronary Constriction. Pflüger's Arch. ges. Physiol. **261:** 41 (May), 1955.

The arterial and venous pressures in the systemic and in the pulmonary circulation were recorded in 8 dogs. The effects of acute constriction or occlusion of the right coronary artery, or of the circumflex branch of the left coronary artery, were studied. Stenosis of the right coronary artery causes an increase of the right atrial pressure and a synchronous fall in pulmonary artery pressure. These effects are interpreted as being due to right ventricular failure secondary to ischemia. Later, the aortic pressure also falls without increase of left atrial pressure. This results from the decrease in cardiac output caused by right cardiac failure.

Partial or complete occlusion of the left circumflex artery results in left ventricular failure. The left atrial pressure is increased, and the aortic pressure falls. The decrease in left ventricular output also produces a fall in the right ventricular output. It i

concluded that in acute, severe ischemia the intercoronary anastomoses do not compensate effectively for the marked reduction in myocardial blood flow. The diversion of blood through the anastomoses is not sufficient to cause ischemia and failure of the cardiac muscle normally served by vessels that have not been occluded.

CALABRESI

Kuo, P. T., and Joyner, C. R., Jr.: Angina Pectoris Induced by Fat Ingestion in Patients with Coronary Artery Disease. J. A. M. A. **158:** 1008 (July 23), 1955.

The authors observed a drop in the oxygen-tension readings of exposed myocardium in the dog following a slow intravenous injection with a fat-emulsion preparation. These observations suggested that in human beings the chylomicrons of postprandial lipemia might exert a similar influence that could be demonstrated especially in patients whose myocardial blood supply was already compromised by severe coronary disease or aortic valvular disease. Most authors have assumed that the increased incidence of anginal pain after meals is due to increased cardiac work and reflex vasoconstriction of the coronary arteries. By giving the patient a fat meal that was small in volume and slow in absorption, the authors were able to minimize the early effect of the meal on the circulation of the patient with severe coronary disease, and still to induce lipemia in 14 patients with angina pectoris. Six of the patients developed a total of 14 typical attacks of angina pectoris while at rest 3 to 5 hours after the ingestion of such a meal. None of the patients showed subjective or objective evidence of coronary insufficiency shortly after the meal. Attacks of anginal pain occurred invariably at, or near, the peak of the lipemic curve. This study indicates that postprandial lipemia may exert a deleterious effect on the myocardium of patients whose coronary circulation is already severely compromised. For this reason, a low-fat diet may well be useful in the management of patients with angina pectoris. The lipemia-induced angina pectoris has provided an opportunity for the study of the effects of various drugs and diets upon symptomatic coronary artery disease.

KITCHELL

Gofman, J. W., Lindgren, F. T., Strisower, B., deLalla, O., Glazier, F., and Tamplin, A.: Cigarette Smoking, Serum Lipoproteins, and Coronary Heart Disease. Geriatrics **10:** 349 (Aug.), 1955.

Levels of serum lipoproteins for men between the ages of 20 to 29 years, 30 to 39 years and 40 to 49 years were collected with respect to those who never smoked, those who smoked fewer than 10 cigarettes daily, 10 to 19 cigarettes daily, 20 or more daily and those who were pipe or cigar smokers. Similar data were collected for women from 18 to 39 years of age, except that there were no pipe and cigar-smoking groups. Significant elevation in levels of lipoprotein classes S_f 0–12, S_f 12–20, S_f 20–100, S_f 100–400, was noted in association with regular cigarette smoking, particularly in young men. The association of cigarette smoking with lipoprotein elevation leads to the prediction of a 40 per cent increase in mortality from coronary heart disease in regular cigarette smokers as compared with nonsmokers.

RINZLER

Holzmann, M.: Experiences with the Rudimentary Anterior Wall Infarction. Am. Heart J. **50:** 407 (Sept.), 1955.

"Rudimentary anterior wall infarction" is characterized by the onset of severe attacks of angina pectoris, which are not unduly prolonged as in status anginosus, normal temperature, leukocyte count and sedimentation rate. The QRS complex is not altered, but the RS-T and T wave exhibit changes in the same leads as are seen during the evolution of an anteroseptal infarction. The RS-T is elevated and the T wave is inverted most markedly in the region between the left sternal border and the apex. The prognosis for this syndrome is favorable. The report is based on a study of 80 cases, 65 male and 15 female. The ages ranged from 50 to 65 years of age. Some patients experience recurrent angina.

RINZLER

CONGESTIVE HEART FAILURE

Higgins, J. A., Juergens, J. L., Bruwer, A. J., and Parkin, T. W.: Loculated Interlobar Pleural Effusion Due to Congestive Heart Failure. Arch. Int. Med. **96:** 180 (Aug.), 1955.

An analysis of 41 cases shows that in 26 (63.4 per cent), the effusions were located in the right transverse fissure alone, and that in another 6 cases (14.6 per cent), the site of effusion was in the right transverse and right oblique fissures. Thus, the transverse fissure was involved in 78 per cent of cases. One reason for this preponderance may be that loculated effusions at this site are more readily discovered on routine posteroanterior roentgenograms, since the rays pass through the greatest diameter of the mass of the effusion. Effusions in the oblique fissure on each side are best seen on lateral views.

Most authors believe that a loculated, interlobar effusion occurs when obliterative pleuritis makes the remainder of the pleural space unavailable for the accumulation of fluid. That this is not always the case is proved by reports in the literature illustrating the occurrence of a free pleural effusion subsequent to the appearance of a collection of fluid in the interlobar spaces. Only rarely do these patients give a history of pleurisy. Repeated accumulations of pleural fluid are thought by some authors to play

an etiologic role in certain cases by producing an obliterative pleuritis.

BERNSTEIN

Hayward, G. W.: Pulmonary Oedema. Brit. M. J. **1:** 1361 (June 4), 1955.

Acute pulmonary edema is most commonly due to left ventricular failure from hypertension, coronary artery disease, aortic valve disease, and mitral stenosis. In an interesting group it follows cerebrovascular accident or fracture of the skull. Early in the attack no adventitious sounds except possibly asthmatic wheezes may be present in the lung, in spite of intense dyspnea. Later, bubbling rales and coughing of frothy sputum develop. Occasionally, the usual pain of myocardial infarction may be absent and acute pulmonary edema may be the first manifestation. If there is no history of previous exertional dyspnea, and if the blood pressure drops rather than rises during the acute attack, myocardial infarction is a likelihood.

The factors responsible for development of pulmonary edema are fundamentally the same as those at other sites. Pulmonary capillary pressure, as measured by catheter impaction, is 5–10 mm. Hg. The osmotic pressure of plasma is 25–30 mm. Hg. In animals, lung-lymph contains appreciable protein, so that effective capillary osmotic pressure in the lung may not be more than 20 mm. Hg. Clinical and experimental evidence supports neurogenic control of capillary permeability. Up to a certain point the lymphatics can carry away fluid from the interstitial space between the capillaries and the alveoli. The thickening of the alveolar wall, representing increased tissue between the capillary and the alveolus, may impede the development of pulmonary edema in cases of chronic left ventricular failure or mitral stenosis.

From his own experience and that of others, Hayward collected a total of 23 cases of mitral stenosis and pulmonary edema with cardiac catheterization in six of which studies were performed before and during the attack. Pulmonary artery pressure and pulmonary capillary pressure rose. No case of pulmonary edema occurred in a case of very high pulmonary vascular resistance. Resistance tended to fall during the attack. The pulmonary artery-pulmonary capillary pressure gradient is usually unchanged. Both rise during the attack.

Anoxia may augment and perpetuate pulmonary edema through its effects on capillary permeability. Experiments purporting to show increased pulmonary capillary permeability following injection of substances into the floor of the fourth ventricle have been shown to be accompanied by rise in left atrial pressure. So neurogenic factors are still *sub judice*.

In mitral stenosis, increase of heart rate by 10 or 15 points may so shorten diastole that pulmonary capillary pressure will rise dangerously. There is no proof as yet for the interesting idea that the pulmonary veins constrict actively, the "pulmonary venous throttle mechanism," in pulmonary edema.

Attacks of pulmonary edema may have their onset in sleep, if the orthopneic patient slips down in bed, if he makes a sudden movement as in turning over after a period of muscular relaxation and increases venous return thereby, and if there is an increase in heart rate as a result of nightmare.

The efficacy of venesection and tourniquets is easy to understand. Aminophylline may help by relieving bronchospasm. Morphine may slow the heart rate by allaying anxiety, reducing venous return by relaxing skeletal muscle, diminishing muscular activity and reducing cardiac output through reduced metabolic demand.

Acute digitalization with Digitoxin has been reported to produce acute left ventricular failure through its pressor effect.

Evidence is presented that dyspnea in left-sided failure is usually the result of interstitial pulmonary edema with reduced pulmonary compliance. The lung is rendered more rigid than normal. This reaches its ultimate in acute pulmonary edema in which is found sticky mucinous fluid in the airways and bronchial narrowing by spasm, edema or swelling of pulmonary bronchial anastomotic veins.

McKUSICK

Sharpey-Schafer, E. P.: Effects of Valsalva's Manoeuvre on the Normal and Failing Circulation. Brit. M. J. **1:** 693 (March 19), 1955.

In 62 normal persons and 63 patients with heart failure, continuous arterial pressure recordings were made while the subject blew a column of mercury to 40 mm. and maintained it at that level for 10 seconds.

The Valsalva maneuver causes acute reduction in effective filling pressure of the heart. In normal persons decrease in arterial pulse pressure was followed by a rise in diastolic pressure (overshoot). In heart failure of any cause, there was usually no change in pulse pressure and no overshoot. The overshoot phenomenon was explained on the basis of peripheral vasoconstriction in response to the decreased pulse pressure.

It is claimed that the effects of the Valsalva maneuver can be detected at the bedside by feeling the pulse. It may be useful in determining whether or not heart failure is present, but is of no use in following the progress in cases of established heart failure.

McKUSICK

Lutterotti, M.: Electrophoretic Protein Shifts in Heart Failure. Arch. Kreislaufforsch. **22:** 170 (May), 1955.

Alterations of blood proteins and their fractions in the course of heart failure were investigated in 100 patients, with paper electrophoresis. The ma

terial was grouped according to the type of heart failure and evaluated on the basis of statistical principles.

In over-all heart failure, including primarily older patients with degenerative heart disease, and in combined right and left ventricular failure, a marked increase of γ-globulins was found, and this more frequently than in the other groups. The β-and α-globulins were elevated to a lesser degree, the latter in particular when heart failure was advanced. The albumins, on the other hand, were reduced. Predominant right heart failure showed a similar behavior, although alterations of γ-globulins and of albumin were less pronounced. In predominant left heart failure, no significant changes of the blood proteins were present unless the failure was severe, under which circumstances the albumins were slightly lower and the α-globulins increased.

In general, it appeared that the amount of edema did not significantly influence the blood-protein pattern. Diureses caused further reduction of the albumin fraction and a transient rise of γ-globulin. The shift in the protein composition seems to be related rather to the duration of liver congestion. In addition to hepatic factors, inflammatory processes associated with heart disease, the age of the patient, and malnutrition seem to participate in the constellation of the blood proteins in congestive heart failure.

PICK

ELECTROCARDIOGRAPHY, VECTORCARDIOGRAPHY AND BALLISTOCARDIOGRAPHY

Trethewie, E. R. and French, E. L.: Electrocardiographic Studies of Experimental Murine (Mem) Virus Myocarditis. M. J. Australia **1:** 817 (June), 1955.

Electrocardiographic studies were carried out on mice inoculated with MEM virus. The electrocardiograms showed lengthened PR interval, bradycardia, ST depression, and, in the more severe grade, typical infarct patterns.

Autopsy studies were confirmatory of electrocardiographic findings. In one instance, in which a large dose of inoculum was given, electrocardiographic changes were found before histologic abnormalities were evident.

BERNSTEIN

Blasius, W., and Repger, R.: Vectorial Analysis of the Chest Electrocardiogram with Regard to the Eccentric Position of the Heart in the Chest. Pflüger's Arch. f. d. ges. Physiol. **261:** 8 (May), 1955.

Mathematic formulation and geometric construction are presented to correct the chest electrocardiographic leads for the eccentric position of the heart. A fixed anatomic location of the zero point is adopted; reference is made to studies in progress, in an effort to establish the zero point in each subject. A single dipole and a homogeneous medium are assumed. Bipolar leads, from the apices of 2 equilateral triangles at the level of the fourth intercostal space, are obtained; the 2 mean QRS and T vectors are constructed according to the classic formulation (Einthoven-Canfield). The discrepancy in magnitude and in direction between the pairs of vectors obtained by this construction is significantly reduced if the proposed correction is adopted. This is taken as evidence of the validity of the formulation presented.

CALABRESI

Cahen, P., Froment, R., Lehmann, M., and Pont, M.: Restitution of the T Wave in Right Precordial Leads Following an Exercise Test in Mitral Stenosis. Arch. mal. coeur **44:** 820 (Sept.), 1955.

In cases of mitral stenosis, exercise causes inverted T waves in right precordial leads to become upright. In 18 instances this change occurred invariably in leads V_2 and V_3, and in one half of the cases in V_1. It is not caused by an associated tachycardia, changes of neurovegetative tone, or modification of the position of the ventricles during exercise. Alteration of the repolarization process could be due to ischemia of the subendocardium of the right ventricle, which in turn is effected by changes in hemodynamics of the pulmonary circulation upon exercise. Thus, a secondary abnormality of T waves attributable to right ventricular hypertrophy is converted during exercise to a primary abnormality, caused by acute coronary insufficiency. An objection to this interpretation is the failure of ischemic T-wave alterations to occur in acute cor pulmonale.

PICK

Friese, G.: The Esophagoatriogram in Normal and in Cardiac Patients. Arch. Kreislaufforsch **22:** 288 (Aug.), 1955.

A new method is described of registration of atrial pulsations in the esophagus using an infrasound recorder. The method was applied in 57 normal persons and 157 patients with heart disease.

In normal persons the amplitude of the pulsation depends on the width of the retrocardial space, the body position, the phase of respiration, and the duration of the A-V conduction time. In mitral insufficiency the pattern is characterized by the occurrence of a "reflux" wave replacing the normal wave of atrial inflow. It is most marked in incipient mitral regurgitation and becomes less pronounced with progressive dilatation of the atrium. In mitral stenosis 3 types of abnormal deflections can be distinguished. These are characterized by augmentation of the atrial contraction wave (type I), by a flattening of the descending portion of the filling wave (type II), and by addition of a ventricular systolic plateau (type III). Correlation with findings at cardiac surgery suggested that type I corresponds

to a mild mitral stenosis and the other 2 types to tight stenosis. In combined mitral stenosis and regurgitation the 2 corresponding patterns are mixed, yet it is possible to detect in the esophagoatriogram signs of regurgitation that acoustically may be silent. Atrial fibrillation may change these characteristic features from variations of the duration of diastole and superposition of flat fibrillation waves. In incipient left heart failure the atrial contraction wave at first becomes larger and is followed by a diastolic plateau; in later stages of failure, the atrial contraction wave is absent. Similar alterations are described in chronic cor pulmonale and, in the author's opinion, are due to pressure elevation in the left atrium caused by concomitant left heart failure.

This method may in the future be useful in the assessment of operability of cases with mitral disease without using cardiac catheterization.

PICK

Hartmann, I., Veyrat, R., Wyss, O. A. M., and Duchosal, P. W.: Vectorcardiography as Studied on the Isolated Mammalian Heart Suspended in a Homogeneous Volume Conductor. Cardiologia **27:** 129 (Fasc. 3), 1955.

Isolated and perfused cat hearts were suspended in the center of a spherical container filled with conducting fluid, and unipolar electrocardiograms were recorded from various positions within the conducting medium. The purpose of the study was to determine (a) the minimal distance at which opposite scalar leads can be considered symmetrical and (b) the characteristic configuration of comparative vectorcardiograms when the electrodes are brought closer to the heart.

Balanced, that is, mirror-image, scalar electrocardiograms as well as reliable vectorcardiograms can be obtained from points removed from the surface of the heart at distances at least twice the diameter of the heart. With such an arrangement the curves reflect, to the same extent, size and orientation in space of the over-all electric activity to which each part of the myocardium contributes. Positions nearer the heart result in progressive distortion of scalar records and vectorcardiograms attributable to so-called partial-lead effect, which gradually develops into intrinsic or focal effects as recorded from circumscribed points of the surface of the heart.

PICK

ENDOCRINE EFFECTS ON CIRCULATION

Chapman. E. M., and Maloof, F.: The Use of Radioactive Iodine in the Diagnosis and Treatment of Hyperthyroidism: Ten Years' Experience. Medicine **34:** 261 (Sept.), 1955.

This review is based upon the experience at the Massachusets General Hospital, where since 1943 585 patients with hyperthyroidism have been treated with radioactive isotopes of iodine.

The authors discuss various tests of thyroid function and conclude that the most informative are the I^{131} uptake, serum protein-bound iodine, and the basal metabolic rate.

Dosage of I^{131} is fairly well standardized at about 0.160 mc. per Gm. of estimated thyroid weight. Originally, the treatment was given only to patients over 45 years old, but subsequently younger patients were included. The treatment is not given in pregnant women beyond the fourth month.

The clinical response to I^{131} was a gradual return of metabolic processes toward normal. The basal metabolic rate returned to normal, usually in 2 months. Radiation sickness did not occur. Myxedema occurred in 8 per cent, usually after 4 months, but in some cases, as long as 8 years later. About 75 per cent of the cases responded to a single dose. Only 11 per cent required more than two doses. There was only 1 case of recurrence of hyperthyroidism, and this was in a nodular goiter. The authors found no evidence to support the use of antithyroid drugs after I^{131} therapy, and in fact, believe that their use may be contraindicated.

The clinical response of thyrocardiac patients tended to be slower than noncardiac patients. In 12 out of 27 patients with atrial fibrillation normal rhythm occurred without the use of quinidine when the patient became euthyroid; in 8 cases, fibrillation persisted. The patients with severe heart disease usually responded favorably to I^{131} therapy, despite the fear of release of preformed hormone into the circulation after internal radiation. Myxedema should be avoided in these cardiac cases.

The question of carcinoma of the thyroid attributable to internal radiation is still unsettled. Since carcinoma develops in 0.4 per cent of patients with exophthalmic goiter, a significantly higher incidence than this will be necessary before I^{131} can be incriminated.

ENSELBERG

Jones, R. J., Cohen, L., and Corbus, H.: The Serum Lipid Pattern in Hyperthyroidism, Hypothyroidism and Coronary Atherosclerosis. Am. J. Med. **19:** 71 (July), 1955.

Mean total lipid, total cholesterol, and phospholipid levels were all significantly higher in 17 myxedematous patients than in 25 hyperthyroid patients. The beta lipoprotein and faster rising lipoprotein moieties showed a particularly striking increment as contrasted with an insignificant difference in the alpha lipoproteins. The increase of the serum lipids in patients with hypothyroidism is qualitatively indistinguishable from that seen in idiopathic hypercholesterolemia, which is so often associated with coronary atherosclerosis. Hypercholesteremic patients in comparison with hypothyroid patients matched as to sex, age and cholesterol level, showed

a significantly higher beta lipoprotein fraction group. Atherosclerosis appears, therefore, to produce hyperlipemia by a different mechanism from myxedema. The observation is also consistent with the idea that the primary abnormality of the serum lipids in atherosclerosis is an elevation in the level of beta lipoprotein.

HARRIS

Russ, E. M., Eder, H. A., and Barr, D. P.: Influence of Gonadal Hormones on Protein-lipid Relationships in Human Plasma. Am. J. Med. **19:** 4 (July), 1955.

Gonadal hormones modify the concentration and distribution of plasma lipoproteins as measured by the Cohn micro-fractionation method. Estrogens usually reduce abnormally high levels of beta lipoproteins suspected of inducing atherosclerosis. Androgens elevate them persistently despite concurrent estrogen therapy. Reversion of the plasma lipoproteins toward normal continues only so long as estrogens were administred. Physical and psychologic manifestations of gonadal therapy made protracted therapy difficult. Estrogen therapy caused dramatic disappearance of tuberous xanthomatous deposits in a case of primary hypercholesterolemic xanthomatosis with hyperlipemia while estrogen was given. In 2 cases of nephrosis, chemical changes qualitatively similar to those observed in survivors of myocardial infarction were perceptible but were so small as to be therapeutically insignificant.

These observations appear significant in the pathogenesis of atherosclerosis. They indicate a chemical reason for the relative immunity of young women to the complications of atherosclerosis. They suggest that estrogenic substances might be beneficial in atherosclerotic persons exhibiting striking protein-lipid abnormalities. While the observations have certain therapeutic implications, they indicate side actions that will make estrogens unacceptable to many patients.

HARRIS

HYPERTENSION

Zintel, H. A., Sellers, A. M., Jeffers, W. A., Mackie, J. A., Hafkenschiel, J. H., and Lindauer, M. A.: A Three to Seven Year Postoperative Evaluation of 76 Patients with Severe Hypertension Treated by Thoracolumbar Sympathectomy. Surg., Gynec. & Obst. **101:** 48 (July), 1955.

A follow-up study was made on a series of 76 patients with severe hypertension, on whom rather extensive bilateral extirpation of the splanchnic nerves and ganglionated sympathetic chain had been performed. The over-all mortality, including that associated with the operative procedure, was 30 per cent. In this number, males predominated.

The length of life of the operated patients was prolonged as compared with a control group of non-operated individuals. Poor renal function was the most important contraindication to operation. Following surgery, neither progressive impairment nor improvement of renal function was noted. Relief of congestive heart failure, angina pectoris and headache was observed in the majority of the patients that could be attributed to the operation.

ABRAMSON

Moore, C., and Birchall, R.: Unusual Case of Hypertension Due to Unilateral Pyelonephritis. Ochsner Clinic Reports. **1:** 25 (July), 1955.

Nephrectomy for unilateral renal disease with hypertension has resulted in improvement in 19 to 45 per cent of reported cases. In the authors' series of 25 cases the 2-year "cure" rate was 48 per cent. The original criteria for selecting the patients for nephrectomy were found to be misleading. A case of hypertension due to unilateral renal disease in a girl 15 years of age, apparently cured by nephrectomy, was presented. Uric acid stones presumably resulted in the pyelonephritis, which produced atrophy of the right kidney and secondary hypertension. The occurrence of falsely positive histamine and "Regitine" reactions for pheochromocytoma is noteworthy, particularly since the histamine reaction was negative after the atrophic kidney was removed. A meticulous search of the removed specimen failed to reveal any evidence of a pheochromocytoma.

BERNSTEIN

Lee, R. E.: Hemodynamic Changes in the Bulbar Conjunctival Capillary Bed of Subjects with Hypertension Associated with "Cushing's Syndrome" or Pheochromocytoma. Am. J. Med. **19:** 203 (Aug.), 1955.

The capillary bed in the bulbar conjunctiva was studied in 8 patients with hypertension associated with pheochromocytoma or "Cushing's disease." In hypertension caused by pheochromocytoma there is a similar but less notable vasoconstriction than in essential hypertension, less hyperreactivity to epinephrine and complete absence of capillary and venular coiling, tortuosity, and elongation. During a hypertensive crisis, extreme increase in vasoconstriction, tissue ischemia, and reactivity to epinephrine was observed in contrast to the stability of the vascular status in essential hypertension.

Individuals with hypertensive vascular disease display the following functional and morphologic changes in the capillary bed of the bulbar conjunctiva: (1) vasoconstriction of the minute terminal arterioles and metarterioles, (2) increased reactivity of these vessels and the precapillary sphincters to topically applied epinephrine, (3) reduction in the velocity of peripheral blood flow and (4) a prominent change in vascular topography; namely, elongation, coiling, and tortuosity of the true capillaries, particularly of their distal and venular portions.

HARRIS

Maloney, J. M.: Pheochromocytoma in Pregnancy. Cesarean Section and Adrenalectomy. New England J. Med. **253:** 242 (Aug. 11), 1955.

A woman, aged 24 years, with pheochromocytoma diagnosed during her second pregnancy is described in detail. Characteristic paroxysmal attacks began in the third trimester of the pregnancy. The paroxysms were controlled with phentolamine, and the patient was delivered by cesarean section. During this surgical procedure, the pheochromocytoma was located in the left adrenal gland. One week following the cesarean section, adrenalectomy was performed. The patient was prepared with cortisone, norepinephrine, and epinephrine in oil, and the last 2 drugs were used postoperatively. Microscopically, the tumor was characteristic of pheochromocytoma. Although other instances of pregnancies coexisting with pheochromocytoma have been recorded, this is believed to be the first in which the diagnosis was made antepartum.

ROSENBAUM

PATHOLOGY

Scotti, T. M.: Basophilic (Mucinous) Degeneration of the Myocardium. Am. J. Clin. Path. **25:** 994 (Sept.), 1955.

Basophilic degeneration of myocardial fibers occurs frequently but is seldom reported. The lesion is characterized by basophilic appearance of myocardial fibers stained with hematoxylin and eosin. Histochemical studies support the belief that the substance is mucinous.

The incidence of basophilic degeneration of the myocardium in a series of 75 consecutive autopsies was 71 per cent. It occurred most commonly in the left ventricle, less often in the interventricular septum and was observed also in the right ventricle in both atriums and in both atrial appendages. The lesion was noted most commonly in patients over 40 years of age.

Basophilic degeneration occurs frequently in hearts with abundant lipochrome pigment. In the present study, certain cardiovascular lesions were noted frequently in association with basophilic degeneration of the myocardium, and the possible relation of these lesions is discussed.

BERNSTEIN

PATHOLOGIC PHYSIOLOGY

Lodin, H. and Thoren, L.: Renal Function Following Aortography Carried out under Ganglion Block. Acta radiol. **43:** 345 (May), 1955.

Some aortographies are followed by evident renal damage, usually reversible. Most of the changes in the various clearances can be abolished by general anesthesia, or by a systemic ganglionic blocking agent, such as tetraethyl ammonium bromide (Etamon) employed in this series.

Tests of renal function were performed in 15 patients before and after aortography, and no evidence for residual renal damage was noted. One patient had temporary renal failure, but later renal function tests indicated no residual damage.

SCHWEDEL

Smythe, C. M. and Gilmore, J. P.: The Effect of Morphine on Hepatic Blood Flow in the Normal Anesthetized Dog. J. Pharmacol. and Exper. Therap. **114:** 221 (June), 1955.

Current clinical practice discourages the use of morphine in patients with liver disease. This clinical aphorism, plus scattered laboratory observations, suggested a study of the effects of morphine on hepatic hemodynamics.

Estimated hepatic blood flow (EHBF) was determined by the BSP removal method (Bradley, 1945) in 14 anesthetized dogs before and after 1 mg./Kg. of morphine tartrate, intravenously. There was no significant change in EHBF, splanchnic oxygen consumption, splanchnic resistance, hepatic venous unsaturation and hematocrit. Hyperventilation, a marked fall in arterial pressure and an increase in the depth of narcosis occurred.

These studies do not elucidate the mechanism for the clinical taboo on the use of morphine in patients with liver disease.

WECHSLER

Werkö, L., Ek, J., Varnauskas, E., Bucht, H., Thomasson, B. and Eliasch, H.: The Relationship Between Renal Blood Flow, Glomerular Filtration Rate and Sodium Excretion. Cardiac Output and Pulmonary and Systemic Blood Pressures in Various Heart Disorders. Am. Heart J. **49:** 823 (June), 1955.

The cardiac output and blood pressures in the pulmonary and systemic circulation were determined simultaneously with the renal clearances for inulin and para-aminohippurate in 146 cases of various heart diseases. They consisted of 34 patients with congenital heart disease, 7 patients with primary pulmonary disease, 4 with constrictive pericarditis, 2 with polycythemia, 15 with hypertensive cardiovascular disease, 12 with aortic valvular disease and 72 with mitral valvular disease. The renal blood flow was lower than normal in all cases with cardiovascular disease, roughly proportional to the severity of the heart disease. The decreased renal blood flow was usually found together with decreased stroke volume, but elevated renal venous pressure seemed to contribute to the decreased blood flow not at all or only a little. Studies during exercise also pointed to the minor importance of the elevated venous pressure for the renal changes. The renal blood flow increased to normal when a case with patent ductus was surgically corrected, and towards normal in a case with atrial septal defect and pulmonary stenosis when the defect was closed. When cases with mitral

stenosis were operated on, the renal blood flow showed variable changes, although a slight increase usually was found when the pulmonary circulation was improved. When isotonic glucose was infused at a rate of 25 ml./min., the renal blood flow increased to normal in cases with mitral stenosis or pulmonary fibrosis. The sodium excretion increased successively to several times the basal value. This reaction is the same as in cases with arterial hypertension and is not found in normal individuals. These findings indicate that cases with heart disease prone to develop congestive failure, long before any signs of failure have appeared, exhibit changes in renal circulation and sodium handling.

RINZLER

McKusick, V. A., Kay, J. H., and Isaacs, J. P.: Constrictive Pericarditis Following Traumatic Hemopericardium. Ann. Surg. **142:** 97 (July), 1955.

The authors reported a case of constrictive pericarditis that developed 18 months after a gunshot wound of the heart. Initially, a left thoracentesis had been performed with the removal of a large quantity of grossly bloody material. About one month later, a second pericardial tap was done and a smaller quantity of fluid was obtained.

The patient was asymptomatic until about a year and a half after the trauma, when he became dizzy on exertion and even lost consciousness on one occasion. Reexamination revealed a change in roentgenkymograms, suggesting constrictive pericarditis. At thoracotomy, the heart was found totally encased in a dense fibrous scar averaging 6–8 mm. in thickness. As this material was dissected from the heart, considerable ballooning of the ventricles occurred. The patient made an uneventful recovery.

ABRAMSON

Best, M. M., Duncan, C. H., Van Loon, E. J., and Wathen, J. D.: Effects of Sitosterol on Serum Lipids. Am. J. Med. **19:** 61 (July), 1955.

In 14 patients on free diets to whom 20 to 25 Gm. of sitosterol were administered daily for prolonged periods, a sustained lowering of serum total cholesterol resulted. A concomitant reduction in serum total lipid, neutral fat and, to a lesser degree, lipid phosphorus occurred. A trend toward lower levels of S_f 3–10, 10–30, and 30–100 classes of lipoproteins also occurred, but less consistently than the reduction of serum cholesterol. The effects of sitosterol are attributable to its interference with absorption of cholesterol. They are not identical with those of dietary cholesterol restriction, since sitosterol seems to reduce absorption of cholesterol present in the bile as well as that present in the diet. It is suggested that sitosterol interferes with cholesterol absorption by competing for esterification, a step in the transport mechanism by which cholesterol is absorbed. The changes in serum lipids and lipoproteins resulting from sitosterol administration are in the direction generally considered desirable in atherosclerosis. The absence of any toxic or adverse side-effects permits its further study in man.

HARRIS

Hatch, F. T., Abell, L. L., and Kendall, F. E.: Effects of Restriction of Dietary Fat and Cholesterol upon Serum Lipids and Lipoproteins in Patients with Hypertension. Am. J. Med. **19:** 48 (July), 1955.

Serum lipid and lipoprotein levels were observed in hospitalized patients with severe essential hypertension undergoing both partial (23 patients) and practically complete (44 patients) restriction of dietary fat and cholesterol. Restriction of dietary fat to 3 Gm. per day and elimination of cholesterol intake did not reduce the serum lipid or lipoprotein levels in any patient below normal. Carbohydrate and protein appear to be ready sources for endogenous synthesis of the lipids present in the serum. Drastic dietary restriction of fat and cholesterol affected the serum lipid patterns with great variability. Serum cholesterol ester levels usually declined with restriction of daily fat intake below 40 Gm. Free cholesterol and lipid phosphorus concentrations showed no consistent change. Dietary restriction did not significantly alter the concentration of the S_f 12–20 class of lipoprotein particles and substantial increases in the S_f 20–100 class were provoked. The response of the serum lipids and lipoproteins was not predictable for any given patient. The type of change observed was not correlated with the severity of the hypertension or with the presence or absence of arteriosclerotic complications. The restriction of dietary fat rather than the restriction of dietary cholesterol is responsible for the observed alterations of the serum concentrations of cholesterol and other lipids. The study supports the general thesis that total caloric intake is of greater significance in relationship to maintenance of serum lipid and lipoprotein levels than the quantity of cholesterol or of fat ingested.

HARRIS

Mann, G. V., Munoz, J. A., and Scrimshaw, N. S.: The Serum Lipoprotein and Cholesterol Concentrations of Central and North Americans with Different Dietary Habits. Am. J. Med. **19:** 25 (July), 1955.

The investigators found significantly lower serum cholesterol levels but no consistent difference in serum lipoprotein levels of rural Central American subjects on a vegetarian low-fat diet compared with urban Central and North American subjects on a liberal fat intake. There was little evidence of the typical North American increase of serum cholesterol level with age among these rural Central Americans. The beta-lipoproteins of the females in

the rural group were frequently at higher levels than those of the North Americans. The urban Guatemalans showed lipoproteins as high or higher than those of the North American group.

These cholesterol- and lipoprotein-level differences could not be explained by the greater leanness of the Central Americans. The greater leanness of the rural Guatemalan group taken with higher caloric consumption of that group, suggests that the serum lipoprotein levels may be dependent upon the magnitude of energy turnover, whereas the serum cholesterol levels are increased by energy accretion or fat deposition. The differences in dietary fat intake among the groups do not serve to explain the serum lipid differences because they do not permit an explanation of the dissociation of cholesterol and lipoprotein measurements, which is unique in the rural Guatemalans.

HARRIS

Kuipers, F.: Chronic Constrictive Pericarditis Combined with Hypoproteinaemia. Arch. Dis. Childhood **30:** 285 (June), 1955.

The author presents a case of constrictive pericarditis in a 7-year-old child. Although the physical signs suggested the diagnosis, it was not confirmed by the routine investigations. The radiokymograph revealed good pulsations. Cardiac catheterization was suggestive and calcium was demonstrated in the pericardium with "heavily burnt" x-ray. Marked hypoproteinemia was present and its association with constrictive pericarditis is discussed. A successful pericardectomy was performed.

HARVEY

Freeman, O. W., Mitchell, G. W., Wilson, J. S., Fitzhugh, F. W., and Merrill, A. J.: Renal Hemodynamics, Sodium and Water Excretion in Supine Exercising Normal and Cardiac Patients. J. Clin. Invest. **34:** 1109 (July), 1955.

The clinical improvement and disappearance of edema in some cardiac patients treated with bed rest alone suggest that exercise is a potentiating factor in sodium retention. In this study, renal hemodynamics were studied in 15 control and 11 cardiac subjects. Postural effects were excluded by exercise in the supine position.

No consistent change in sodium excretion or glomerular filtration rate was noted during exercise among normal persons or compensated cardiac patients. However, the filtration rate, renal plasma flow, and sodium excretion fell significantly when patients in congestive failure performed the exercises. Sodium excretion fell to an average of 38 per cent of the control value.

WAIFE

Judson, W. E., Hatcher, J. D., Hollander, W., and Halperin, M. H.: The Effects of Mitral Valvuloplasty on Cardiovascular and Renal Function at Rest and During Exercise. J. Clin. Invest. **34:** 1297 (Aug.), 1955.

Little information is available on renal hemodynamics or electrolyte excretion in the early period following mitral valvuloplasty. In this report, 9 patients with mitral stenosis were studied before and after valvuloplasty. The operation produced varying degrees of improvement in cardiovascular and renal functions, both at rest and after exercise, and in none, however, did the hemodynamics return to normal. Although a general improvement in cardiovascular function was sometimes associated with increases in renal plasma flow, glomerular filtration rate, and the ability to excrete salt and water with exercise, postoperative increases in salt and water excretion could not be consistently correlated with any *specific* change in cardiovascular or renal function.

WAIFE

PHARMACOLOGY

Jindal, M. N.: Cardiovascular Toxicity of Quinine and Quinine Calcium Gluconogalactogluconate in Experimental Animals. J. Indian M. A. **25:** 52 (June), 1955.

The effects of quinine and a quinine calcium compound (calcium gluconogalactogluconate) on the cardiovascular system of the dog were compared. The quinine calcium compound lowered the blood pressure of dogs less than quinine itself. Quinine depressed the myocardium, while quinine calcium compound, in big doses, was a stimulant. Thus, quinine calcium compound is considered a safe drug for parenteral administration.

BERNSTEIN

Page, E.: Precipitation of Ventricular Arrhythmias Due to Digitalis by Carbohydrate Administration. Am. J. Med. **19:** 169 (Aug.), 1955.

Administration of carbohydrate orally or intravenously in 7 patients at, or near, the point of digitalis intoxication, precipitated ventricular premature beats in 6 patients and ventricular tachycardia in 1 patient. This effect is attributed to reduction in the arterial plasma potassium level after administration of carbohydrate.

HARRIS

Lensen, J., Demeester, G., and DeWitte, Jr.: Influence de l'Acetyl-Digitoxine-sur le Muscle Papillaire du Chat. Arch. internat. pharmacodyn. **102:** 153 (June), 1955.

The therapeutic and toxic dosage of acetyldigitoxine is studied by measuring its effects upon the contraction, in an aqueous medium, of an isolated papillary muscle from the right ventricle of a cat. By means of an ingenious recording system, the shortening of the muscle is observed. The therapeutic concentration was about one fifth the toxic concentration in the aqueous bath. These

relations were similar to others measured by other investigators previously.

HARVEY

Malinow, M. R., Battle, F. F., and Malamud, B.: The Pharmacology of Experimental Ventricular Arrhythmias in the Rat. Arch. internat. pharmacodyn. **102:** 55 (June), 1955.

Ventricular flutter and fibrillation were produced in anesthetized rats by intravenous injection of a 10 per cent solution of calcium chloride, previously shown to be mediated by neurogenic mechanisms, or by application, through the open chest of an artifically respired rat, of aconite upon the epicardium of the right ventricle, clearly cardiogenic. The cardiac rhythm was observed by means of the electrocardiogram or direct vision. The protection from these arrhythmias afforded by prior intravenous administration of various antihistamine drugs, namely, Antistine, Benadryl, Fenergan, Pyribenzamine, and Neo-Antergan, was measured. The studies were well controlled. Both neurogenic and cardiogenic arrhythmias could be prevented, but all the antihistamine drugs were not equally efficacious, Antistine and Benadryl being the most active, and Neo-Antergan the least active. A discussion of possible mechanisms is presented.

HARVEY

Von Euler, U. S.: Noradrenaline in Hypotensive States and Shock. Lancet **2:** 151 (July 23), 1955.

Noradrenalin is present in large amounts in vessel walls and in such organs as spleen, skin, heart and kidneys. Furthermore, there is a relationship between the natural concentration of this material in a given organ and degree of response to infused noradrenalin. In man about 16 per cent of the catecholamines of the adrenal medulla is noradrenalin and the rest adrenalin.

Noradrenalin raises systolic and diastolic pressure without affecting cardiac output. Adrenalin raises cardiac output with little effect on mean pressure because of vasodilatation in skeletal muscle. Effect of the two drugs on renal vascular resistance is about the same, but blood flow is increased by noradrenalin because of increase in blood pressure.

Noradrenalin, like adrenalin, speeds the isolated heart but the effect is likely to be masked in the intact organism by reflex bradycardia. Even in high dosage noradrenalin causes coronary vasodilatation. There seems to be less ectopic excitation and less wasteful oxygen consumption with noradrenalin.

Total oxygen consumption is raised 20 to 30 per cent by adrenalin but virtually unaffected by noradrenalin. Similarly, noradrenalin has little effect on blood sugar, lactic acid, eosinophiles and the psyche.

Contrary to previous views, the sympathetic nervous system and the adrenal medulla have different physiologic roles. Two types of secretory cells are present in the adrenal medulla, each with its own mechanism for nervous stimulation and each capable of stimulation and secretion independent of the other. Carotid occlusion and tilt-table experiments in man result in secretion predominantly of noradrenalin by the adrenal gland.

Adrenalin seems to play a role as the fight-fright-flight emergency hormone, whereas noradrenalin occupies that of the physiologic pressor hormone.

Use of noradrenalin in cardiogenic shock, particularly before ineversibility sets in as a result of loss of vascular reactivity, is entirely rational.

MCKUSICK

Lottenbach, K., and Wegmann, A.: The Action of Noradrenaline on the Heart Rate and Its Interpretation. Cardiologia **27:** 135 (Fasc. 3), 1955.

One of the known effects of noradrenalin in man is bradycardia, which usually is ascribed to a reflex mechanism mediated by pressor receptors. However, the authors found that when noradrenalin was injected in small amounts (0.014–0.14 γ per Kg.) in healthy young persons bradycardia was produced without rise in blood pressure, and that this bradycardia could not be prevented by atropine sulfate or ganglionic-blocking agents. To explain these observations several assumptions can be made. One could be a direct effect of noradrenalin on "vagal substances" in the heart. If the hypothesis of a reflex mechanism is to be maintained, one would have to postulate either that afferent vagal impulses are transmitted over ganglia resistant to pharmacologic agents or that noradrenalin enhances afferent vagal impulses as well as efferent ones.

PICK

Wakim, K. G.: Certain Cardiovasculorenal Effects of Hexamethonium. Am. Heart J. **50:** 435 (Sept.), 1955.

In the anesthetized dog, the effects of intravenously administered hexamethonium chloride were studied on the renal blood flow, urine production, cardiac output, heart rate, and the systemic and pulmonic blood pressures. The influence of vagal stimulation on the heart rate, respiration, and blood pressure was compared before and after administration of the drug. Renal blood flow was measured directly by a flowmeter connected between the renal vein at the hilus of the kidney and the central end of the distally ligated femoral vein. Thus, renal venous blood passed through the flowmeter to the vena cava via the femoral vein. Cardiac output was determined by the Fick principle. Systolic-diastolic pressures from the systemic and pulmonic systems were recorded on photosensitive paper by use of strain gages connected to cardiac catheters.

Intravenously injected hexamethonium chloride caused considerable reduction in cardiac output and prolonged reduction in blood pressure and renal blood flow. These circulatory changes were accompanied by marked reduction in formation of urine. Hexamethonium caused a slight increase in renal resistance. The cardiac standstill and the precipitous fall in blood pressure, produced by stimulation of the vagus nerves, were abolished after administration of hexamethonium. The action potentials recorded from afferent impulses, obtained from stretch receptors in the lungs, were not affected by the administration of hexamethonium.

RINZLER

Clark, B. B., and Etsten, B.: Pharmacologic and Antiarrhythmic Actions of Ambonestyl (2-Diethylaminoethyl-isonicotinamide) in Man. Preliminary Report. New England J. Med. **253:** 217 (Aug. 11), 1955.

In experimental studies, Ambonestyl (2-Diethylaminoethyl-isonicotinamide, MC4112) had ventricular antiarrhythmic activity as great as procaine amide or quinidine, but had less depressive effect upon cardiac conduction and less hypotensive activity. Observations were made in 8 unanesthetized patients and on 8 additional patients before or during surgical procedures. When administered intravenously and rapidly in unanesthetized or lightly sedated patients in doses of 100 mg., repeated at 10 minute intervals to a total dose of 500 mg., there was no appreciable effect. Three injections of 250 mg. each, at 10 minute intervals to a total of 750 mg., resulted in a transient depression of the T wave in the electrocardiogram and a slight, transient increase in heart rate. With doses of 500 and 750 mg. a short sensation of warmth was reported. The drug decreased total peripheral resistance slightly. In 1 patient with partial atrioventricular heart block, the degree of block was decreased by the drug: in no case was there depression of cardiac conduction. Persistent hypotension did not occur although a transient, moderate fall in blood pressure, lasting 1 to 3 minutes occurred after large doses of Ambonestyl were given rapidly. No significant changes in cardiac output were observed. When used in 6 patients with premature ventricular contractions, it suppressed the arrhythmia in all instances. In general, larger doses were required for a persistent suppression of the arrhythmia. Ambonestyl was administered to 2 patients during the serious cardiac operations of mitral commissurotomy and removal of an intra-atrial tumor. The drug was considered of definite value in controlling the ventricular ectopic activity and in maintaining a more normal cardiac function during the operation. The authors believe that Ambonestyl may have some advantages over procaine amide or quinidine, and that it may be of particular value in the treatment of patients with conduction disturbances, in controlling arrhythmias during anesthesia and in patients undergoing cardiac surgery.

ROSENBAUM

PHYSICAL SIGNS

Read, J. L., and Porter, W. B.: The Efficacy of Carotid Sinus Pressure in the Differential Diagnosis of Triple Rhythms. Am. J. Med. **19:** 177 (Aug.), 1955.

Carotid sinus pressure with consequent slowing of the heart rate caused the accessory sound in gallop rhythm to become inaudible and to disappear from the sound tracing in 85 per cent of 13 cases. Whereas, the true gallop sound invariably became inaudible when the ventricular rate slowed below an average "critical rate" of 91, other types of extra sounds became more obvious because of changes in timing, intensity, or clarity. A classification of 3-sound rhythms is presented with a detailed acoustic, physiologic, and clinical discussion of each.

In conditions that alter the valves, vibrations result that have been termed murmurs. In conditions that alter muscular function, notably left or right ventricular failure, an additional sound may appear during diastole that is commonly termed a gallop sound. It is almost invariably associated with a failing ventricle and tachycardia. A gallop sound usually consists of 1 to 7 coarse vibrations of very low frequency; a murmur consists of finer, more regular, and more numerous vibrations. Additional sounds may occur during systole but these are usually of no clinical significance and should not be called gallop sounds. Extra sounds during both diastole and systole may be confused with splitting or reduplication of the first or second heart sound, particularly at rapid rates. The term triple rhythm, or 3-sound rhythm, has been introduced to encompass conveniently all of these various extra heart sounds.

In 1888, Rouches described the opening snap of the mitral valve and suggested that the sound was produced by the sudden stretching of a stenosed mitral valve as the blood rushed from left atrium to left ventricle. This extra sound is important, since it indicates the presence of a flexible or operable valve. It is generally not present in the event of gross calcification of the valve, slight stenosis, or marked insufficiency.

HARRIS

Harned, H. S. Jr., Crothers, C. H., and Whittemore, R.: Diagnosis of Atrial and Ventricular Septal Defects. Am. J. Dis. Child. **90:** 211 (Aug.), 1955.

This is an authoritative study from the Grace-New Haven Community Hospital of the records of 240 children observed over an eight year period

with atrial and ventricular septal defects. Common clinical features were gracile habitus, precordial bulging, transient cyanosis with exertion and crying and diastolic murmurs in the pulmonic area, presumably indicating pulmonic insufficiency.

Ventricular septal defects can be benign in infancy, with good compensation, small hearts and no incapacity. Physical development is impeded under the age of 2 years, but then proceeds normally. Subacute bacterial endocarditis is not so threatening as in adult life. The size of the defect and pulmonary hypertension usually determine the severity of symptoms. The chief clinical feature is the intense, harsh systolic murmur located in the fourth or fifth interspace, left of the sternum.

The atrial septal defect was asymptomatic more often than not. Patients are subjected to repeated pulmonary infections. Abnormal rhythm usually does not develop until late childhood. The differentiation of these abnormalities from many others, including anomalous venous return, mitral valve deformities, atypical patent ductus arteriosus is difficult, but some of the distinguishing features are presented. In discussing catheterization studies, the authors point out that danger from air embolism is less in using the saphenous vein and that a significant increase in oxygen saturation at the tip of the catheter is of great diagnostic value.

HARVEY

Taylor, S.: Cardiophony of the Exposed Heart. Lancet **2:** 380 (Aug. 20), 1955.

An electronic stethoscope, with readily sterilizable parts for application to the surface of the heart and great vessels during thoracotomy, is described. The control box is readily portable and has a built-in loud speaker. The nature of the microphone and other specific details of design are not given. How "feedback" is avoided is not clear.

McKUSICK

Dock, W., Grandell, F., and Taubman, F.: The Physiologic Third Heart Sound: Its Mechanism and Relation to Protodiastolic Gallop. Am. Heart J. **50:** 449 (Sept.), 1955.

Graphic registrations of events associated with the third heart sound and protodiastolic gallop generally agree in showing that these sounds occur at the very end of the rapid inflow to the ventricles, and that they are associated with an apical thrust and rate of fall of venous pressure greater than when there are no such sounds.

Roentgen studies of the left border of the heart show that the ventricular expansion is completed at about the time the sound occurs.

The present study on 6 young men confirmed these facts and showed once more that the intensity of the normal third sound varies with respiration and posture. The sharpness of the apical thrust and of the jugular reflux varied with the intensity of the sound. The headward or rightward thrust of the body in ballistocardiograms, which is a striking accompaniment of most gallop sounds from diseased hearts, was seen only with the loudest third sounds. The direction of this wave shows that the force causing the sound is acting, not from the atrium toward the ventricle, as would be the case if the sound was due to tensing the ventricular walls, but in the opposite direction. Only in constrictive pericarditis is the heart in a condition of altered distensibility when the third sound occurs, and the normal hearts of men and dogs may show constant volume for the latter two thirds of diastole, even when this volume varies from cycle to cycle with respiration.

Because the valves are drawn taut at the moment reflux begins, after rapid inflow ceases, and because the valves are easily set into audible vibration, while the flabby ventricular wall is not a suitable structure for emitting sounds, it is concluded that the third sound and gallop sounds originate when the atrioventricular valves are forcibly tensed by a reflected wave.

The earliest gallop or third sound falls at the same time in the heart cycle as the latest opening mitral snaps. As a general rule, normal third sounds vary widely during each respiratory cycle, while the opening snap and gallop vary but little from one heart beat to another. In small or normal-sized hearts third sounds may occur 0.12 second after the second sound; in graphic records of single cycles they are indistinguishable from normal third sounds. Records made during normal breathing usually differentiate an opening snap, a gallop, and a normal third sound.

RINZLER

PHYSIOLOGY

Bartels, H., Beers, R., Fleischer, E., Hoffheinz, H. J., Krall, J., Rodewald, G., Wenner, J., and Witt, I.: Determination of Circulatory Shunt and of Diffusing Capacity of the Lung in the Normal and in Pulmonary Disease. Pflüger's Arch. ges Physiol. **261:** 99 (June), 1955.

Oxygen pressure, oxygen content, oxygen capacity, carbon dioxide content, alkali reserve, pH of arterial and venous blood, and the respiratory volume and RQ were measured in 9 normal persons. The alveolar oxygen pressure, the alvelo-arterial oxygen-pressure difference, the cardiac minute volume, the arteriovenous pulmonary shunt, and the diffusing capacity of oxygen were calculated. These data were obtained on individuals breathing ambient air, hypoxic (12.2 per cent), and hyperoxic (34.7 per cent) mixtures. The procedures and the results are evaluated and estimates of methodologic errors

are presented. Two examples are reported from a group of patients with pulmonary disease.

CALABRESI

RHEUMATIC FEVER

Markowitz, M., and Kuttner, A. G.: The Effect of Intensive and Prolonged Therapy with Cortisone and Hydrocortisone in First Attacks of Rheumatic Carditis. Pediatrics **16:** 325 (Sept.), 1955.

The authors presented a thorough study of the effects of steroid treatment in 40 children in the first attack of rheumatic carditis. Daily doses of 300 mg. of cortisone were given orally. Penicillin was given to all during the whole period of treatment. Treatment was started in 29 of the patients within 3 weeks of the onset of the attack. Seventeen of the patients had severe carditis, defined by the authors as either pericarditis, cardiac enlargement with effusion, or cardiac enlargement with congestive failure. In a follow-up period of 6 to 22 months, 24 of the 29 patients treated early had no evidence of heart disease, whereas in the group of 11 with treatment 3 weeks after onset, only 2 had normal hearts, 8 had definite rheumatic heart disease, and 1 had died in severe congestive failure. The authors believe that large amounts of cortisone given early enough and for a long enough time will suppress the inflammatory response and the subsequent scarring. They point out that their study is not statistically significant but is suggestive and that further investigation should be conducted.

HARVEY

Editorial: Natural History of Mitral Stenosis. Lancet **2:** 329 (Aug. 13), 1955.

Until recently the principal nonoperative study of the natural history of mitral stenosis was a 10 year follow-up by Grant (1933) of 238 men who served in World War I. Forty-two per cent of these men died in 10 years.

During the current year, Olesen has reported from Denmark (published by Munksgaard) a study of 351 patients with mitral stenosis followed from 3 to 20 years. Two hundred seventy-one of the patients had only this valvular lesion, but a history of rheumatic infection was recorded in 58 per cent. Mitral stenosis was detected at ages from 14 to 73 years. The median from the onset of symptoms to death was 18 years, but the range was wide. After the onset of atrial fibrillation, only 50 per cent survived 6 years and 10 per cent 16 years.

Of patients with dyspnea on mild exertion (American Heart Association Classification, Grade II) and sinus rhythm, 70 per cent survived for 20 years; at that time cardiac status was unchanged in 40 per cent. Of patients in class III with sinus rhythm, or in class II with atrial fibrillation, 46 per cent survived 10 years and 11 per cent survived 17 years. Grade IV dyspnea (total incapacitation) and congestive failure occurred on an average of 15 years after onset of symptoms. Thereafter, over 50 per cent died within 1 year and 95 per cent died within 7 years. Wood, P., (1954) estimated the average to be a 7-year interval between onset of symptoms and incapacitation. The average age at death was 47 years.

The widely variable course of mitral stenosis may be related to the unpredictable degree of continuing activity of the rheumatic process. Only patient and prolonged observation will establish the precise role of valvulotomy in the management of this disease.

MCKUSICK

Samlert, H., and Gassler, R.: Roentgenologic and Functional Pulmonary Alterations in Mitral Stenosis. Ztschr. Kreislaufforsch. **44:** 641 (Aug.), 1955.

The relationship of cardiodynamics to the degree of pulmonary vascular markings in the roentgenogram was investigated in 103 cases of mitral stenosis. In most of the cases, changes in right ventricular pressure and arterial oxygen content and in pulmonary vascularization were associated. The authors imply that hyperventilation and alterations in the amount of arteriovenous pulmonary shunts account for their findings.

PICK

Tosetti, R. L.: Resistance Zones in the Pulmonary Circulation in the Course of Mitral Stenosis and in Chronic Cor Pulmonale due to Emphysema. Arch. mal. coeur **48:** 346 (April), 1955.

A concept is presented of the mechanisms involved in pulmonary hypertension, based on histologic studies of pulmonary vessels in normal persons and in patients with mitral disease and with pulmonary emphysema. Different "zones of resistance" are assumed to be present in the pulmonary circulation according to the appearance and pathologic alterations found in successive vascular segments.

In mitral disease, 3 pathologic stages can be recognized. The initial stage consists of venospasm of small veins. In an intermediate stage the vasospasm is generalized and involves arterioles with hypertrophy of the vessel walls. In the terminal stage there is obliterative sclerosis with degeneration of the wall and loss of elastic elements. In all 3 stages, the capillaries and smallest arterioles and venules are unaffected or even dilated. In pulmonary emphysema, on the other hand, the zone of resistance is at the level of vessels of smallest caliber, which are reduced in number and show anatomic changes. The author considers direct stimulation of pressure receptors in the venous segment of the pulmonary circulation as the primary pathogenic

factor responsible for the anatomic vascular alterations encountered in mitral disease.

PICK

Van den Heuvel-Heymans, G. M.: Pressure Curves of the Left Atrium. Intracavitary and Esophageal Registrations. Their Value in the Diagnosis of Mitral Defects. Acta cardiol. **10:** 115 (Fasc. 2), 1955.

Pressure variations may be measured in man in he esophagus at the level of the left atrium by means of a balloon filled with fluid connected to a recording device by polyethylene tubing. Curves obtained in this way were compared with direct left atrial pressures obtained during thoracic operations. Both types of pressure curves showed the same characteristics under normal and abnormal conditions, provided that the filling pressure of the esophageal balloon was kept higher (20–50 mm. Hg) than the intracavitary pressure.

Pressure curves in normal and abnormal conditions were described. The various waves in the esophagogram and the atriogram differed in timing, amplitude, and origin. Calculations of certain relationships of the esophageal deflections led to formulas for the correct diagnosis of a mitral lesion, particularly that of mitral regurgitation. The method is simple and more reliable than other technics used for this purpose.

PICK

Ruberman, W., and Hoffman, M. J.: Aortic Insufficiency among Young Adults. Am. J. M. Sc. **230:** 197 (Aug.), 1955.

During a period of 30 months, rheumatic valvular disease was found in 61 soldiers at an Army training and reception center. Of this group, 33, or 54 per cent, had aortic insufficiency. There were 5 with aortic stenosis, 8 with mitral stenosis, and 18 with mitral insufficiency. All with aortic insufficiency were between 20 and 25 years of age, and 70 per cent had a history of acute rheumatic fever prior to induction. Collateral signs of aortic insufficiency were detected in one third. The electrocardiogram was normal in all but one instance. The usual presenting symptom was dyspnea induced by heavy exertion. Frequently, chest pain occurred after exertion. The difficulty in detecting the murmur of aortic insufficiency and the need for a painstaking examination are emphasized.

SHUMAN

Bishop, J. M., Donald, K. W., and Wade, O. L.: Changes in the Oxygen Content of Hepatic Venous Blood During Exercise in Patients with Rheumatic Heart Disease. J. Clin. Invest. **34:** 1114 (July), 1955.

In this study of 14 patients with rheumatic heart disease, profound and rapid increases in the hepatic arteriovenous oxygen difference occurred during leg exercise in the supine position. The increase was greatest in patients with severely limited cardiac output in response to exercise.

The low oxygen saturation in hepatic venous blood in these cases indicates that the liver, especially the centrilobular cells, is subjected to very low oxygen tensions during exercise. A resulting necrosis or cardiac cirrhosis is postulated.

WAIFE

ROENTGENOLOGY

Cregg, H. A., Smith, P. W., Wilson, C. W., and Bull, J. W.: Cardioangiography. Radiology **65:** 368 (Sept.), 1955.

The authors report 8 patients in whom 20 ml. of 70 per cent Diodrast was injected directly into the ventricle by the subxiphoid approach, presumably as in the 3 illustrated cases into the left ventricle. One of the 8 patients developed ventricular fibrillation lasting for 3 minutes before sinus rhythm was restored by cardiac massage. No significant complications were encountered in the other 7 patients.

The authors believe that better opacification obtained by this method should lead to the more accurate diagnosis of congenital and acquired lesions of the heart and great vessels. Thus far they have not undertaken such injections in adults with cyanotic heart disease or in children.

Previously, the authors had carried out 60 ventricular punctures in 13 dogs by the subxiphoid route. In 1 dog the dye was accidentally injected into the myocardium and death from ventricular fibrillation resulted; in another, the left lobe of the liver was lacerated; in 2, some dye was injected into the pericardium; in 2, transient gross hematuria developed. In 15 other dogs the intercostal approach was used, but it was abandoned after a coronary vessel was lacerated and cardiac tamponade resulted.

SCHWEDEL

Steinbach, H. L., Keats, T. E., and Sheline, G. E.: The Roentgen Appearance of the Pulmonary Veins in Heart Disease. Radiology **65:** 157 (Aug.), 1955.

The authors discuss the appearance of the pulmonary veins in roentgenograms taken in the usual posteroanterior and oblique views, occasionally with the aid of tomograms. They conclude that the size of the veins generally correlates well with the amount of pulmonary blood flow. Large veins occurred in intracardiac left-to-right shunts, patent ductus arteriosus, and aortic-pulmonary window. Small pulmonary veins were found in pulmonic stenosis, tetralogy of Fallot, and pulmonary artery thrombosis. In one instance, the presence of large pulmonary veins in a patient with evident pulmonic stenosis

was due to the associated patent ductus arteriosus plus anomalous entry of a pulmonic vein into the right atrium.

In mitral stenosis the normal or diminished size of the pulmonary veins was ascribed to pulmonary venous constriction or to compensatory organic narrowing or vasoconstriction of the smaller branches of the pulmonary artery.

SCHWEDEL

SURGERY AND CARDIOVASCULAR DISEASE

Kirtley, J. A., Jr., Riddell, D. A. and Hamilton, E.: Indications and Late Results of Inferior Vena Cava Ligation. Ann. Surg. **141:** 633 (May), 1955.

On the basis of a study of 34 patients in whom inferior vena caval ligation had been performed for thrombo-embolic disease, the authors arrived at certain conclusions regarding indications for this operation and the effects which follow it.

Among the indications for the procedure are the presence of conditions which prevent the use of anticoagulants, repeated pulmonary infarction, progressive thrombosis of the lower extremity above the inguinal ligament with pulmonary embolism, trauma to the inferior vena cava and septic pelvic thrombophlebitis. It is the authors' opinion that any venous ligation at a level lower than the inferior vena cava is not justified.

Among the late disabling sequelae of inferior vena caval ligation are severe edema, ulceration, dermatitis and pain. These are found in only a small percentage of patients.

ABRAMSON

Glenn, F.: Indications and Contraindications for the Surgical Treatment of Mitral Stenosis. Ann. Surg. **141:** 686 (May), 1955.

The author discusses the criteria for the proper choice of patients for mitral commissurotomy and the various contraindications to this procedure. One of the most important indications is progressive disability. Of value in determining whether this exists is the determination of the general physical status and the state of the heart. In regard to the latter point, roentgenographic studies, including angiocardiography, electrocardiography and cardiac catheterization are very helpful.

Ideally the patient should have no or only a minimal degree of mitral insufficiency associated with the stenosis. In general, the younger the individual and the shorter the history since the first episode of rheumatic fever, the more satisfactory will be the correction of the stenosis of the mitral valve.

Among contraindications to the operation are bacterial endocarditis, clinically active rheumatic fever, severe mitral regurgitation and severe involvement of other valves. Calcification of the mitral valve is not interpreted as a contraindication to operation. Demonstration of primary renal disease is an indication for caution and individualization in preoperative preparation and postoperative management.

ABRAMSON

Mazel, M. S.: Persistence of New Vascular Channels Following Cardiopericardiopexy. J.A.M.A. **158:** 36 (May 7), 1955.

In a case of chronic coronary disease treated by cardiopericardiopexy, autopsy 15 months later showed that the vascular channels were still patent in the pericardial adhesions. Death had been caused by rupture of an aortic aneurysm. Since some writers have considered the beneficial results following cardiopericardiopexy to be temporary, because newly formed vascular channels and granulation tissues have a tendency to regress, it is interesting to note that the vascular channels produced by operation in this patient had remained patent for at least 15 months.

KITCHELL

Kirklin, J. W., DuShane, J. W., Patrick, R. T., Donald, D. E., Hetzel, P. S., Harshbarger, H. G. and Wood, E. H.: Intracardiac Surgery with the Aid of a Mechanical Pump-Oxygenator System (Gibbon Type): Report of Eight Cases. Proc. Staff Meet., Mayo Clin. **30:** 201 (May), 1955.

In a series of operations upon eight patients who had severe congenital heart disease, each with symptoms of advanced severity indicating a poor prognosis, the mechanical pump-oxygenator system adequately maintained the patients during the period of perfusion. Use of this system established excellent conditions for precise, unhurried intracardiac surgery. The foregoing facts demonstrate the usefulness of this technic in the surgical treatment of certain abnormalities of the heart and great vessels.

SIMON

Poth, E. J., Childers, J. H., Johnson, J. K. and Guy, R. S.: Vascular Replacements and Reconstruction Utilizing Inert Material. Am. J. Surg. **89:** 1196 (June), 1955.

The authors utilized prostheses constructed from raw nylon to reestablish the continuity of arteries in dogs and in one human subject with an arteriovenous fistula. In the experimental study, gross and microscopic examinations of the implant were made at various periods after operation.

The early changes consisted of the migration of plasma, red blood cells and leukocytes through the wall and into the surrounding spaces between the layers of the graft and the adjacent tissues. These were followed by the formation of a thrombus covered by a layer of leukocytes.

Later, a more compact arrangement of blood cells and degenerated elements was included in the

thrombus, associated with dilatation and some proliferation of the small capillaries in the perivascular tissues adjacent to the outer surface of the prosthesis. Migration of fibroblasts occurred between the bundles of nylon fibers.

The authors concluded that on the basis of their work, as well as that of others, the use of pervious, flexible tubes tailored from inert plastic materials for replacement of segments of arteries is worthy of further study. According to them, the prosthesis serves as inert scaffolding into which viable host-tissues grow, the material also acting as reinforcement to prevent dilatation of the host-tissues under the prolonged arterial pressures.

ABRAMSON

Felder, D. A., Murphy, T. O. and Ring, D. M.: A Posterior Subfascial Approach to the Communicating Veins of the Leg. Surg., Gynec. & Obst. **100:** 730 (June), 1955.

The authors describe an operation for ligation of incompetent communicating veins which they performed upon 28 patients with long-standing venous stasis. The procedure consists of making a longitudinal incision on the posterior aspect of the leg, extending from the popliteal fossa to the level of the malleoli and separating the fascia from the muscles. In the course of this dissection, all communicating veins are ligated as they emerge from the muscle to penetrate the fascia.

On the basis of their results, the authors believe that any patient who suffers from the lower-limb stasis syndrome and whose disease manifestations are not controlled by conservative measures may benefit from posterior subfascial venous ligations.

ABRAMSON

THROMBOEMBOLIC PHENOMENA

Rosenman, L. D. and Gropper, A. N.: Small Intestine Stenosis Caused by Infarction: An Unusual Sequel of Mesenteric Artery Embolism. Ann. Surg. **141:** 254 (Feb.), 1955.

The authors present a case of mesenteric artery embolism, which caused an infarct of the small intestine, leading to cicatrization and stenosis. They pointed out that if certain favorable circumstances prevail, acute intestinal ischemia is not lethal. Among these is the rapid development of an adequate collateral circulation, arterial, venous or both, before bacterial penetration of the ischemic intestine occurs. Another important factor is the prevention of a reduction in cardiac output.

ABRAMSON

Millikan, C. H., Siekert, R. G. and Shick, R. M.: Studies in Cerebrovascular Disease. III. The Use of Anticoagulant Drugs in the Treatment of Insufficiency or Thrombosis within the Basilar Arterial System. Proc. Staff Meet., Mayo Clinic. **30:** 116 (March), 1955.

This is the first report of the use of anticoagulant drugs in the treatment of a group of patients suffering from a specific variety of intracranial vascular disease. Such drugs were administered to five patients suffering from intermittent insufficiency of the basilar arterial system and to 21 patients suffering from thrombosis within the basilar arterial system. During treatment, in all instances, the attacks suffered by the five patients in the first group ceased. Three patients of the second group died, giving a mortality rate of 14 per cent for this group. The mortality rate for a group of untreated patients was 43 per cent.

The length of time anticoagulant drugs should be administered is not known. It is emphasized that the general danger of anticoagulant therapy has been carefully assessed in each instance and the use of such treatment sharply limited to specific categories of intracranial vascular disease.

SIMON

Jamison, W. L., Rao, K. V. S. and Bailey, C. P.: Pulmonary Embolism following Mitral Commissurotomy. With Special Reference to a Subvalvular Type. Am. J. Surg. **89:** 272 (Jan.), 1955.

The authors present typical cases of pulmonary embolism and discuss the type in which the clot is lodged in the right ventricle below the level of the pulmonic semilunar valve (subvalvular). The latter entity is associated with intermittent recurrent cyanosis which does not respond to oxygen therapy, probably because the clot acts as a ball valve, intermittently extending from the right ventricle, where it does not produce obstruction, to the pulmonic valve, where it does. Other findings are hypotension which does not respond to vasopressors, tachycardia, out of proportion to any evidence of cardiac failure, and a high white blood count.

It is believed that the site of origin of pulmonary embolism, at or after mitral commissurotomy, is most likely from the right atrial appendage.

ABRAMSON

Rosegay, H. and Welch, K.: Peripheral Collateral Circulation between Cerebral Arteries. A Demonstration by Angiography of the Meningeal Arterial Anastomoses. J. Neurosurg. **11:** 363 (July), 1954.

Occlusive thrombosis of the proximal segment of a cerebral artery is not common, and the diagnosis is made clinically more often than justified by either angiographic or autopsy data. As more studies, both from angiography and autopsy, have become available, the impression is gained that cerebral infarction caused by thrombosis is much more often the result of carotid occlusion than of cerebral artery occlusion.

The authors state that, following occlusion of a major cerebral artery, collateral circulation occurs by means of the meningeal arterial anastomoses to

the extent that retrograde filling of the occluded vessel can be seen on angiograms. They describe three such cases. In the first, there was a segmental thrombotic occlusion of the most proximal part of the middle cerebral, and a very adequate collateral circulation from the anterior cerebral is shown. In the second case, the middle cerebral was occluded by a hemostatic clip at a point 1 inch from its origin, and reflux filling of the distal part of the vessel by collaterals from the anterior and posterior cerebrals, is shown. In the final case, in which both anterior cerebrals were occluded, retrograde filling of the callosomarginal artery is shown to occur through the anastomotic branches of the middle cerebral artery. Providing optimal conditions exist, this collateral circulation is effective in taking over the vascular supply of the cortical territory of an occluded vessel.

DENNISON

Sachs, E.: Arteriographic Demonstration of Collateral Circulation Through Ophthalmic Artery in Internal Carotid Artery Thrombosis. Report of Two Cases. J. Neurosurg. **11:** 405 (July), 1954.

Thrombosis of the internal carotid artery has gained considerable attention in recent years and is a diagnosis made with increasing frequency. An associated loss of vision in the homolateral eye has been observed by a number of authors. This was explained by the inadequacy of blood flow through the ophthalmic artery to the retina because of the proximal thrombosis. However, some authors found only a rather modest incidence of blindness and optic atrophy in these patients. This failure of blindness to occur in the homolateral eye has therefore intrigued observers, and the free collateral circulation between the external carotid and ophthalmic arteries has been an explanation for its absence.

Another striking thing about internal carotid thrombosis has been the occasional absence of neurological signs or evidence of massive infarction, even after arteriography has demonstrated complete obstruction of flow of dye into the internal carotid vessels in the neck. The authors present their experience with two cases, bringing to light the fact that in cases of internal carotid thrombosis demonstrable by arteriography, collateral circulation through the ophthalmic artery may be visualized, thereby corroborating previous experimental work presenting this as a explanation for the failure of blindness to occur in the homolateral eye. This same finding, indicating a richness of circulation adequate to fill the intracranial branches of the internal carotid artery, may also account for the paucity of neurological symptoms in some of these cases.

The author's first case demonstrates extraordinary lack of neurologic signs and symptoms, failure of blindness to occur in the homolateral eye, arteriography may reveal collateral circulation about a thrombosis of the internal carotid through the ophthalmic artery back into the intracranial portion of the internal carotid artery and its branches.

The second case, following arteriography, revealed the internal carotid artery ending blindly several millimeters above the bifurcation. A small amount of dye reached the circle of Willis, via retrograde filling through the external carotid and ophthalmic artery and then into the intracranial portion of the internal carotid, where it stopped.

DENNISON

Harder, H. I. and Brown, A. F.: Embolization of Basilar Artery by Myocardial Fragment. Arch. Int. Med. **95:** 587 (April), 1955.

A case is described in which an embolus containing heart muscle lodged in the basilar artery. No reference to a similar case has been found in the standard medical indices. An additional unusual feature is that the embolus was enabled to lodge in the basilar artery because of the congenital enlargement of one vertebral artery.

BERNSTEIN

Foley, W. T., McDevitt, E., Symons, C. and Wright, I. S.: Further Experience with Long-Term Anticoagulant Therapy. Arch. Int. Med. **95:** 497 (April), 1955.

Eighty-five patients with disease characterized by thromboembolic episodes were placed on long-term anticoagulant therapy, from periods of one to eight years (a total of 3552 patient-months). Patients with the following diagnoses were treated: rheumatic heart disease, recurrent thrombophlebitis, myocardial infarction and certain diseases with miscellaneous diagnoses. Thirty-one hemorrhagic episodes occurred, the majority of which were mild. One patient died after a cerebral hemorrhage.

Eighty-five patients, selected as outlined above, observed for a total of 3673 patient-months without anticoagulants, had 290 thromboembolic episodes. During a period of 3552 patient-months on anticoagulant therapy, these same patients experienced 32 thromboembolic complications.

BERNSTEIN

Teplick, J. G. and Yarrow, M.: Arterial Infarction of the Kidney. Ann. Int. Med. **42:** 1041 (May), 1955.

Arterial occlusion of a kidney is a clinical entity and is not uncommon. It usually occurs in a cardiac patient, especially one with atrial fibrillation. It can also result from trauma. The clinical picture is uniform in most cases. The onset is sudden, with abdominal and flank pain, severe and unremitting for from two to four days. Hematuria is present in about one-half the cases; albuminuria is generally found. Fever and leukocytosis occur within 48 hours. All the symptoms and findings gradually disappear in unilateral infarction. The affected kidney loses its function and is not filled on intravenous pyelography.

Retrograde pyelogram reveals a normal urinary tract, even though little or no urine is observed coming from the affected side. In most cases, renal function never returns. Aortography can confirm the nonfilling of the affected renal vessels. Since the occlusion is ordinarily not due to septic emboli, a sterile autonephrectomy results, with gradual shrinkage and atrophy of the renal elements. Surgery is therefore not usually indicated; if hypertension ensues, nephrectomy will prove curative. Two cases of arterial renal occlusion observed by the authors conform strikingly to the clinical picture described above. Both had atrial fibrillation; both had identical onset and symptoms; both developed fever and leukocytosis; both showed a nonfunctioning kidney by intraurography. In both, the retrograde pyelogram was completely normal. Both patients recovered without surgery. Hematuria was seen in only one; aortography in one patient demonstrated the vascular occlusion.

WENDKOS

Watson, D. C.: Anterior Tibial Syndrome Following Arterial Embolism. Brit. M. J. **4927:** 1412 (June 11), 1955.

The author discusses a syndrome consisting of ischemic necrosis of the muscles of the anterior tibial compartment of the leg, with a lesion of the anterior tibial vein and presents two cases in which such changes were noted after arterial embolism. The characteristic findings in this entity are pain, swelling, redness and tenderness in the front of the leg, with inability to dorsiflex the foot and toes. Involvement of the anterior tibial nerve produces paralysis of the extensor digitorum brevis muscle and sensory loss on the dorsum of the foot. In most instances, the anterior tibial syndrome can be related to strenuous unaccustomed exercise involving the use of the leg muscles.

The entity must be differentiated from cellulitis of the leg, osteomyelitis of the tibia, tenosynovitis, acute thrombophlebitis and traction lesions of the lateral popliteal nerve.

With regard to treatment, several approaches may be tried. When there is clinical evidence of raised tension in the anterior tibial compartment, surgical decompression would appear indicated. Means to relieve vasospasm or promote vasodilatation are also worthwhile, particularly in the early stage.

ABRAMSON

VASCULAR DISEASES

de Takats, G. and Lary, B. G.: Traumatic Axillary Aneurysm of Thirteen Years' Duration. Arch. Surg. **70:** 390 (March), 1955.

The authors reported a case of a large axillary aneurysm of 13 years' duration in a 63 year old arteriosclerotic and syphilitic patient. The lesion had been produced by a gunshot wound in the region of the left subclavian artery. Because the aneurysm was very large, it was not resected. Instead it was sidetracked by placing a 10 cm. segment of the cephalic vein between the sectioned proximal and distal portion of the axillary artery. Patency was restored and the large mass gradually became impalpable.

ABRAMSON

Wessler, S.: Studies in Intravascular Coagulation. III. The Pathogenesis of Serum-induced Venous Thrombosis. J. Clin. Invest. **34:** 647 (April), 1955.

SPCA (Convertin or factor VII) is a stable serum factor which accelerates prothrombin conversion. Under the experimental conditions described, massive intravascular thrombosis at sites of retarded and obstructed venous flow was produced by the infusion of serum fractions rich in SPCA. Significant endothelial injury need not be involved. A transient increase in SPCA or other similar blood fraction together with local venous stasis may be responsible for many instances of clinical thrombosis.

WAIFE

Williams, R. R., Bahn, R. C. and Sayre, G. P.: Congenital Cerebral Aneurysms. Proc. Staff Meet., Mayo Clin. **30:** 161 (April), 1955.

A study was made of 172 congenital cerebral aneurysms encountered in 143 cases at necropsy. Almost 90 per cent of these aneurysms arose from the internal carotid arteries and their major branches. Some 37 per cent were located on the anterior cerebral arteries and the short connecting link, the anterior communicating artery. Aneurysms originating from the internal carotid artery comprised 32 per cent of the total. The number of congenital cerebral aneurysms increased progressively from the second to the sixth decade of life. The greatest number of fatal ruptures of aneurysms was in the sixth decade and only 27 per cent of all the patients with aneurysm were beyond the sixth decade of life.

Subarachnoid hemorrhage was the primary complication of rupture of an aneurysm and was the commonest cause of death in the first week after rupture. Intracerebral hemorrhage was present in more than half of the cases in which rupture occurred and was the most frequent cause of death after the first week, when two thirds of the patients with such hemorrhage died. The initial subarachnoid hemorrhage appears to have caused a connective-tissue proliferative reaction which obliterated the subarachnoid space around the aneurysm, so that subsequent bleeding resulted in dissection of the brain itself by the blood. Such subsequent intracerebral bleeding caused rupture into the ventricles in almost three fourth of the cases in which it occurred.

SIMON

Weinstein, L. and Meade, R. H. III.: Idiopathic Thrombophlebitis. Arch. Int. Med. **95:** 578 (April), 1955.

Two cases are described in which prodromal symptoms of backache were followed by severe pain in the thighs and calves, fever, and leucocytosis, without signs of phlebitis in the acute phase. Recovery occurred spontaneously and was followed months later by complete venous occlusion in the legs. In one patient, recanalization of the occluded vessels took place and was complete about seven to eight months after the onset of his illness; in the other, vein ligation and stripping was required one year later because of large varicosities of both legs.

Idiopathic thrombophlebitis is a single disease entity. The various forms which have been described under a variety of names, depending on anatomical location, severity, and outcome, are probably only quantitative variants of the same syndrome.

The cases reported in this paper probably constitute a new syndrome in idiopathic thrombophlebitis, because of the lack of signs of phlebitis in the acute phase of the disease, the long latent period between the onset of the illness and the appearance of signs of venous occlusions and the failure to discover any underlying process which might have been responsible for the venous involvement.

BERNSTEIN

Moore, H. D.: An Evaluation of Venography and Venous Pressures in the Study of the Leg Veins. Brit. J. Surg. **41:** 633 (May), 1954.

The author compared ascending the descending venography with venous pressure readings in 33 legs. In general, all three procedures pointed to the same conclusion. If one was interpreted as demonstrating an unequivocal normal response, the venous tree was considered to be normal. However, if the results with one method were considered abnormal or if there was some question regarding the validity of the changes, then the author felt that the other tests were indicated for support of the conclusions.

The venous pressure was believed to be the most reliable index of the state of the veins. Descending venography was of value in demonstrating the valves in the femoral vein, but a negative result was disregarded on the basis that absence of visualization could have been due to a technical fault as readily as to a fault in the vessel. Ascending venography was considered to be the only way to outline the views of the legs and their valves and the veins of the thigh.

It was concluded that venography should not be the first approach to the study of the veins of the legs, but that it should be used in all cases where the venous pressure readings show a definite abnormality or are doubtful. Ascending venography should be used before descending, the latter being reserved for those cases in which ther is still some doubt after the venous pressures have been taken and ascending venograms have been made.

ABRAMSON

Kettner, M. G., Ferrero, C. and Duchosal, P. W.: Clinical Investigation by the Oscillogram of Peripheral Arteries. Am. Heart J. **49:** 485 (April), 1955.

An analysis of the oscillograms (tracings of arterial oscillations) of the extremities of 127 subjects, both normal and diseased, is presented. Tracings were made with a specially constructed differential manometer based on the principles of the torsion-tension relationship of a twisted metal band and utilizing an ordinary blood pressure cuff. An accurate standardization of the recordings was effected by use of a hypodermic syringe in the pneumatic system. Nitroglycerin was given as a test for vasodilatation. Records were taken with cuff pressure below the level of diastole, before and after medication. A consistent pattern was seen in the ankle oscillograms in the 58 normal subjects studied. The patterns of tracings taken from the fingers and forearms were inconsistent and variable. Of 44 patients with arterial disease, 27 showed abnormally shaped pulse forms in ankle oscillograms. The remainder showed normally or equivocally shaped forms. A number of the 25 patients with various other diseases showed different degrees of abnormality, although most showed normal tracings. No absolute criteria as to timing and size of pulsations, or response to nitroglycerin, could be established, since there was a great overlap between the normal and diseased groups. A brief discussion of the principles involved is presented.

Although more accurate than the clinical determination of the oscillometric index, the oscillogram as recorded by this method is still of limited clinical value. The method promises to be of value in investigative work, by providing an objective measurement of the clinical evaluation of disease states of peripheral arteries, the effects of drugs, and the results of treatment. The manometer described may also be useful in other physiologic and clinical studies.

RINZLER

Clark, R. J., Tousant, E. S. and Sprague, H. B.: Heart Disease in Massachusetts in Relation to the Workmen's Compensation Act. New England J. Med. **252:** 478 (March 24), 1955.

The Workmen's Compensation Act, its administration, the procedures under it and settlement under the act in Massachusetts are reviewed. Six cardiac case decisions under the act are reviewed. In one case in which the medical examiner's opinion was "coronary heart disease," the Supreme Court reversed the decision of the Superior Court and in so doing stated that contrary to the insurer's contention, the occupational strain giving rise to injury need not be an unusual one or the result of heavy work. It is felt that the hub of the problem is concerned with the interpretation of the manner and extent of the aggravation of pre-existing disease by every sort of employment. It is pointed out that the concept of injury has changed so that now employment of itself appears to constitute an injury and giving a man a job seems to be the equivalent of doing him, physically, a disservice.

The authors review recent evidence that suggests that the maintenance of physical exertion over the years acts as a protective mechanism in developing coronary collaterals. It is said that one may argue that unemployment is far worse for the heart than a daily job that is within the capability of the patient. It is the opinion of these writers that coronary atheroma is the price of prosperity, not of industrial employment. In reviewing a case in which the accustomed work was felt to be intensified by emotional stress, the authors mention that this is a factor totally incapable of measurement. It is said that the dangerous admission of nervous strain as the determining factor in death truly opens the floodgates, especially when the court states that such a strain need not be proved, but may be inferred. It is pointed out that decisions are most frequently made without postmortem examination and that without such study, correlation of exertion and damage to the heart or death is at best a most uncertain presumption.

The authors conclude that from the cases reviewed it is becoming clear that no cardiac patient can reasonably expect employment in an occupation covered by the Workmen's Compensation Act. The question is asked, after it is pointed out that 50 per cent of all men over forty-five have some coronary-artery disease, how industry can afford to employ any older workers.

It is concluded that as a result of recent decisions, Workmen's Compensation in Massachusetts in relation to cardiac disease has evolved to a point where it has become in part a sickness insurance for degenerative diseases that are becoming more frequent with the increasing life span. Employers cannot knowingly afford to accept such a liability in a free labor market and, as a result, persons with heart disease and all older persons are being denied needed employment, of which they may be quite capable. Possible corrective measures such as an expert medical panel, waivers, the second injury act, limited payments and substitutive insurance are discussed briefly. Some extension or modification of the latter seems to hold the greatest promise.

ROSENBAUM

McLemore, G. A., Jr. and Levine, S. A.: The Possible Therapeutic Value of Cholecystectomy in Adams-Stokes Disease. Am. J. M. Sc. **229:** 386 (April), 1955.

Cholecystectomy was performed for gallstones on six patients with Adams-Stokes syndrome and one patient with complete heart block without syncopal attacks. The pathogenesis of the cardiac disorder was arteriosclerosis of coronary arteries in five cases, diphtheria in childhood in one case and one case was of congenital origin. There was no operative mortality in this series though three had attacks of asystole during anesthesia. Postoperatively, the incidence of syncopal attacks was decidedly decreased in all instances. In four cases, the improvement was striking as indicated in the case histories. It is believed that reflexes, arising from the diseased abdominal viscus, may produce alterations in heart function and may be partially responsible for syncopal in patients with heart block. The removal of the diseased gall bladder may not only relieve biliary symptoms but may improve the cardiac status in selected cases of complete heart block having attacks of Adams-Stokes syncope.

SHUMAN

Nosik, W. A.: Intracranial Hypotension Secondary to Lumbar Nerve Sleeve Tear. J. A. M. A. **157:** 1110 (March 26), 1955.

The syndrome of intracranial hypotension consisting of nausea, vomiting, stiffness of the neck, occasional fever of variable degree, possibly with extreme prostration and severe headache is well known to anyone experienced in the lumbar puncture. The case of a patient with intracranial hypotension secondary to a laceration to a lumbar nerve sleeve caused by a fall on the buttocks is offered as evidence that such injury with subsequent leakage of the cerebrospinal fluid into the epidural tissue may result from an indirect trauma. It is believed that the cone-like shape of the dural sleeve in the lumbar region at the point of emergence, the pressure wave induced by sudden deceleration of the body, the abrupt change in intra-abdominal pressure caused by tension of musculature and probably some pre-existing weakness of the dural sheath combine to create lumbar nerve sleeve tear in the absence of direct trauma.

KITCHELL

Thompson, C. E. and Malhas, Z. A.: Myxoma of Left Atrium Simulating Mitral Stenosis. Arch. Int. Med. **95:** 614 (April), 1955.

A case of myxoma of the left atrium, simulating mitral stenosis, is presented. The single most significant diagnostic fact is the relentless cardiac failure developing in a short time, albeit other diagnostic features would warrant a diagnosis of rheumatic mitral disease. Sudden changes in position in patients with polypoid intracardiac tumors may aggravate clinical signs and symptoms. This was noted in this case at the time of operation. When cardiac tumors are suspected, it is recommended that changes of position be utilized as part of the examination as well as angiocardiographic visualization of the heart chambers.

BERNSTEIN

Burch, G. E.: Cardiology for the General Practitioner. J. A. M. A. **157:** 1073 (March 26), 1955.

In everyday practice, the major problems of the cardiovascular system that confront the physician are arteriosclerosis, as well as Raynaud's Disease, thromboangiitis obliterans (Buerger's Disease), collagen disease, myocarditis and myocardial degeneration, cardiac dilatation, angina pectoris, coronary thrombosis, intravascular clotting in general, con-

gestive heart failure, shock and cardiac neuroses. Although some advances in knowledge have been made, it is evident that all the major problems remain unsolved. The tendency to use new, unproved gadgets and drugs must be considered objectively in the best interest of the patient. The physician must not neglect or withhold some of the old established procedures to introduce new unproved or even injurious ones. The investigator in his enthusiasm for his own investigations must not fail to delineate clearly the purely investigative from the practical aspects of treatment. The general practitioner may provide the proving grounds for massive testing, but should not be mislead into expecting anything as established for routine clinical use when it is not. This is more important when the measure involves expense to him and the patient, when no definite service and possible harm may be rendered. Failure to maintain a clear perspective is failure to discharge one's responsibilities in research. The general practitioner is in need of exercising a more critical and responsible attitude. Adequate study, perusal of current literature, meditation and reflection are necessary. Time for thought and deliberation are required for the proper approach to the clinical problem and cannot be replaced by routines designed to serve large numbers of patients rapidly and too often unsatisfactorily. The satisfactory and accepted old methods should be learned first and then with adequate awareness of the circumstances new methods may be used gingerly with the necessary caution for clinical trials. They should be accepted and discarded as objectively as they have been investigated. The present era seems to be one of applying something new first and evaluating it later. These comments must not be construed to suggest that medical science should remain static, but rather that more care be exercised when new and unproved methods are introduced into the field of medicine. An important need in the field of cardiovascular disease is better and more hospital facilities for prolonged care of patients with chronic cardiac disease. Separate institutions, portions of institutions or additional beds with adequate ancillary services are needed, especially for patients with myocarditis, myocardial degeneration, cardiac dilatation, chronic ulcers of the leg and foot, slowly reversible cardiac and peripheral vascular disease states. Patients should have greater access to air-conditioned wards, rooms, hospitals and homes for optimal improvement in the hot and humid periods of the year. Hospitalization facilities for the patient with cardiovascular disease are at the same stage as were those for tuberculosis at the turn of the century. The author points out that time, especially for meditation and reflection, is the greatest shortage in medicine today. More of it must be devoted to the patient with cardiovascular disease.

KITCHELL

Ostrove, L. L.: Evaluation of Lumbar Sympathectomy in Advanced Arteriosclerotic Peripheral Vascular Disease Complicated by Gangrene. Am. J. Surg. **89:** 600 (Mar.), 1955.

The author compared the clinical course of two groups of patients with arteriosclerosis obliterans, in one of which lumbar sympathectomy had been performed. He noted that in those individuals whose legs had been sympathectomized, 47.5 per cent required a major limb amputation. In the control non-sympathectomized group, this procedure was necessary in 53 per cent. The difference was not considered significant.

It was concluded that lumbar sympathectomy, as it is currently employed, does not beneficially influence the course of far-advanced peripheral vascular arteriosclerosis complicated by gangrene. However, it may be helpful in delineating the site of amputation below the knee.

ABRAMSON

Pratt, G. H.: Amputation after Surgical Sympathectomy for Obliterative Vascular Disease; Incidence After 309 Sympathectomies. Surg., Gynec. & Obst. **100:** 43 (Jan.), 1955.

The author analyzed the results obtained with 504 sympathectomies performed on 362 patients. Of this number, 309 were done on patients with occlusive arterial disease. In 80 per cent of the latter cases, amputation did not follow sympathectomy despite the fact that the patients in the group were suffering from advanced arteriosclerosis obliterans.

The author concluded that sympathectomy is an excellent ancillary therapeutic measure, provided (1) gangrene is not already present; (2) it is not used to replace the underlying medical management; (3) the patient has a fair chance of surviving the operation; (4) the patient has given evidence of a desire and ability to stop smoking and (5) all other corrective measures for the underlying disease are taken.

ABRAMSON

Beaconsfield, P. and Messent, D.: Blood Flow After General Anesthesia in Sympathectomized Limbs. Anesthesiology **16:** 428 (May), 1955.

In 16 patients who underwent bilateral, cervical or lumbar sympathectomy in separate operations, the hand or foot blood-flow was measured plethysmographically while the patient was under the effects of the general anesthetic agent employed. During cyclopropane anesthesia, the vasodilatation of normal limbs ordinarily observed was also found to be present in sympathectomized limbs, but was of a much lesser degree. This observation substantiates the hypothesis that cyclopropane has a two-fold action on the peripheral vascular system. The major effect is a direct action on the vasomotor centers. This is abolished by sympathectomy. A

lesser effect consists of a local action on the blood-vessel wall which is not interrupted by sympathectomy. With ether anesthesia, no increase in the blood-flow of the sympathectomized limb was observed, although this anesthetic agent did increase the blood-flow of normal limbs. Ether thus has a negligible effect on the peripheral vascular system through the mechanism involving a local action on the blood-vessel wall.

SAGALL

Soffer, A.: Dangers of Inactivity during Automobile Travel. Am. J. M. Sc. **229:** 475, (May), 1955.

The relative immobility imposed upon a 72-year old female during most of a 68-hour bus trip resulted in the formation of pronounced edema of the lower extremities. Following this, she developed several grand mal convulsions which were attributed to cerebral ischemia in the absence of neurologic sequelae or spinal fluid changes. Cerebral blood flow may have been impaired by pooling of blood in the lower extremities. Such vascular stasis has been responsible for a number of instances of thrombotic disease of the lower extremities with pulmonary emboli following automobile travel. It is recommended that automobile riders make frequent stops to permit movement of the legs. In older age groups, leg binders may be used as a precautionary measure.

SHUMAN

Gasner, W. G. and Costello, J. M.: Sponge Rubber Boot for Varicose Eczema and Varicose Ulcers. J.A.M.A. **158:** 181 (May 21), 1955.

The authors report a method of constructing a boot of sponge rubber which can be made quite easily. They report one case with unilateral varicose eczema plus ulcer and one case of bilateral varicose eczema treated successfully by means of this appliance.

KITCHELL

Alvarez, W. C.: The Little Strokes. J.A.M.A. **157:** 1199 (Apr. 2), 1955.

One of the commonest brain lesions, or one of the commonest diseases of man, is that of dozens or scores of thromboses of little arteries in the brain occurring over the course of 10–20 years. The diagnosis of this condition is often delayed because the patient may fail to tell the physician of the bad dizzy spell at the start of his trouble, and also, the physician may not be well enough acquainted with the more bizarre and puzzling symptoms that can result from such little strokes. Slowly over the course of 10–15 years, a person may be pulled down, slowed up, and aged and eventually will die from the lesion.

KITCHELL

OTHER SUBJECTS

Lewis, W. H., Jr., Richardson, D. J. and Gahagan, L. H.: Cardiovascular Disturbances and Their Management in Modified Electrotherapy for Psychiatric Illness. New England J. Med. **252:** 1016 (June 16), 1955.

The opinion is expressed that, although there are no absolute contraindications to psychiatric electrotherapy, certain cardiovascular disorders, particularly recent myocardial infarction, severe congestive cardiac failure, aortic aneurysm, complete heart block and paroxysmal ventricular tachycardia, deserve a cautious approach and possibly delay until there has been improvement in the cardiovascular status. The authors have developed a method designed to reduce the hazard of electrotherapy in patients who are poor risks because of age or advanced cardiovascular disease. The various procedures included in this technic are: (1) pretreatment with Atropine in doses of $\frac{1}{50}$ to $\frac{1}{25}$ grain added to the intravenous barbiturate anesthetic which is begun and continued until just before the application of the electric stimulus; (2) continuous electrocardiography begun just before treatment and continued through recovery; (3) succinylcholine chloride in an average dose of 60 mg. given intravenously as soon as the patient loses consciousness; (4) control of respiration by means of a Guedel type of airway and bag and mask administration of 100 per cent oxygen and (5) electric stimulation applied as soon as the fasciculations induced by the succinylcholine chloride have subsided. The authors have used this technic for a total of 220 treatments in 21 patients, most of whom were poor risks. In 103 treatments, there were cardiac arrhythmias ranging from asystole for 6 or more seconds, ventricular tachycardia or disruption of the cardiac rhythm to scattered ventricular premature beats. The arrhythmia was considered severe or very severe in 34.2 per cent of those patients in whom some disorder appeared. The cardiovascular response to treatment was not always the same in a given patient. The experience with quinidine in this series was inconclusive. Chlorpromazine was used in 35 treatments and seemed to reduce or prevent treatment-induced arrhythmias. The authors found that the paroxysmal rise in arterial pressure following electrotherapy usually lasted ten to thirty minutes and was not prevented by complete myoneural blockade.

Although the changes produced in the outline of the electrocardiogram by electrotherapy were usually slight and transient, there was one patient who developed changes in the T waves which lasted several weeks, and a few patients showed shortening of the P-R interval and prolongation of the QRS complex simulating the Wolff-Parkinson-White Syndrome. The authors express the opinion that succinylcholine is the most suitable myoneural

blocking agent currently available for modification of electrotherapy. The arrhythmias occurring during treatment are classed as vagal and extravagal disturbances according to their origin. Adequate atropinization prevents the former and quinidine and particularly chlorpromazine seem to lessen or prevent the latter.

ROSENBAUM

Millikan, C. H., and Siekert, R. G.: Studies in Cerebrovascular Disease. IV. The Syndrome of Intermittent Insufficiency of the Carotid Arterial System. Proc. Staff Meet., Mayo Clin. **30:** 186 (May), 1955.

Some examples of the literature concerning thrombosis of the internal carotid artery are mentioned. The authors believe that in the literature adequate emphasis has not been placed on the symptoms which frequently precede such thrombosis. It is suggested that these premonitory symptoms make up a syndrome and it is proposed that the name "syndrome of intermittent insufficiency of the internal carotid arterial system" be used. This syndrome consists of intermittent attacks of unilateral impairment of motor or sensory function or both, in certain instances associated with a disorder of speech, homolateral involvement of vision or both. It is suggested that patients having this syndrome be treated with anticoagulant drugs, unless there is some definite contraindication to the use of such therapy.

SIMON

Selzer, A., Bradley, H. W. and Willett, F. M.: A Critical Appraisal of the Concept of Bernheim's Syndrome. Am. J. Med. **18:** 567 (April), 1955.

The authors present a case of a man with hypertensive and coronary heart disease, who suffered from long-standing, systemic, congestive cardiac failure without ever exhibiting significant dyspnea, orthopnea and pulmonary congestion. At necropsy the cardiac septum was deviated to the right, "stenosing" the cavity of the right ventricle. In this case, which fulfills the clinical and pathologic criteria of Bernheim's syndrome, hemodynamic studies revealed the conventional findings of left ventricular failure, pulmonary hypertension and right ventricular failure.

Evidence is presented that the pathologic substrate of Bernheim's syndrome is based upon a misconception, for the cardiac septum normally is deviated to the right, "encroaching" upon the crescentic cavity of the right ventricle, and this relationship appears exaggerated in any heart with a hypertrophied left ventricle, regardless of clinical course. Experimental observations are cited which suggest that the Bernheim concept is inconsistent with present-day knowledge of the mechanics of ventricular function. Cases reported as instances of the Bernheim syndrome apparently represent examples of cardiac failure with conventional dynamic changes in which dyspnea, orthopnea and pulmonary congestive phenomena are inconspicuous. The term, Bernheim's syndrome, should be abandoned.

HARRIS

Bolt, W., and Bell, M. F.: Cardiac Enlargement of Undetermined Cause in Asymptomatic Adults. Am. Heart J. **50:** 331 (Sept.), 1955.

A group of 70 asymptomatic adults, presenting cardiac enlargement by roentgenogram, was studied. No other detectable abnormality was found in these cases, which were followed from 1 to 18 years; 69 were males. The average age of the group was 45½ years, with a range of 22 to 65 years. There were five deaths but no postmortem examinations. The transverse cardiac diameters were increased from plus 13 to plus 24 per cent.

It was postulated by the authors that the enlargement may represent residual cardiac enlargement due to myocarditis from some long-forgotten or unimpressive illness.

RINZLER

Friedman, B., and Olansky, S.: Diagnosis of Syphilitic Cardiovascular Disease with Special Reference to Treponemal Immobilization Tests. Am. Heart J. **50:** 323 (Sept.), 1955.

Observations are reported on treponemal immobilization tests (TPI) in 33 individuals, with lesions of the aorta or aortic valves, in whom standard serologic tests for syphilis were either negative or weakly reactive. In every one syphilitic cardiovascular disease was prominently questioned in differential diagnosis.

The cases were classified on the basis of the clinical impression in 3 etiologic groups: syphilitic, nonsyphilitic, and unknown or uncertain cause. Of 12 patients in the first group the TPI were positive in 9 and negative in 3. Six of the 9 subjects with positive TPI tests had negative standard serologic tests. The unknown-cause group, consisting of 9 patients, had 4 positive and 5 negative TPI tests. None of the 4 patients with demonstrable immobilizing antibody had clinical evidence of syphilis by history, commonly used serologic tests for syphilis, or physical signs, apart from the aortic insufficiency.

No positive TPI reactions were found in the second group of 12 patients, whose disease was clinically judged to be nonsyphilitic in origin.

RINZLER

Bakst, H. J., and Marra, E. F.: Experience with Home Care for Cardiac Patients. Am. J. Pub. Health **45:** 444 (April), 1955.

A two-year study was undertaken to determine the medical-care implications involved in an intensive home-care service for cardiac patients. Two groups of patients were studied who would be clinically, economically, and socially comparable. Subsequent to discharge from the hospital, patients in the study group received individualized care on a 24-hour-a-day, 1-day-a-week call basis in accordance with the best standards of medical practice. Patients were visited at home or seen on an ambulatory basis as indicated by a hospital resident, supervised by a qualified cardiologist and internist. Nursing care at home was provided by the Visiting Nurse Association. No personal contact was made with patients in the control group after discharge from the hospital. These patients received their medical care as ambulatory patients in outpatient departments, by emergency physicians' visits at home, or by subsequent rehospitalization.

Readmission rates, calculated on the basis of 1,000 patients for the period of the study (21 months), indicate that the relative rate of hospital admission for the 2 groups of patients was essentially the same. Readmission to the hospital because of exacerbation of cardiac symptoms, however, occurred over 4 times more frequently in the control than in the study group. On the other hand, hospital readmission for noncardiac disease occurred more than twice as frequently in the study group than in the control group. With a total of 13 deaths in the study group and 10 in the control group, it is apparent that the case-fatality rates showed no significant differences.

The amount of associated disease found in the study group indicates that comprehensive medical-care programs actually increase the variety of services that are needed by groups similar in makeup to the study group. This emphasizes a unique contribution of a home-care program in that it serves a case-finding function in uncovering unsuspected illness and also permits the opportunity for early and accurate diagnosis of incipient concomitant disease. Thus, in the study group of patients, while hospitalization for the manifestations of cardiac disease was markedly reduced, the rate of hospitalization for noncardiac disease was materially increased. The total rate of hospitalization in both groups of patients for all causes, therefore, was essentially comparable, even though the causes of hospitalization and the quality of medical care in each group showed obvious differences.

While the cost of maintaining a patient in his home may be less than the cost of hospitalization, this does not necessarily reduce the over-all cost of medical care. In this experience, the total number of hospital days was approximately comparable in both groups of patients. The provisions of home care for the study group, therefore, served to increase the over-all cost of medical care by the cost of this additional service.

BERNSTEIN

Read, J. L., Bond, E. G., and Porter, R. R.: The Hazard of Unrecognized Catheterization of the Coronary Sinus. Arch. Int. Med. **96:** 176 (Aug.), 1955.

A syndrome resembling myocardial infarction or acute pericarditis may occur following the unrecognized obstruction of a coronary vein during cardiac catheterization. The catheter tip usually appears to have entered the outflow tract of the right ventricle but will not pass further. A procedure is suggested, based on experience with deliberate catheterization of the coronary sinus, which should eliminate this potentially fatal syndrome. The differentiation is based on the appearance of the catheter in the anteroposterior versus the right anterior oblique position, the visible difference in oxygen content of coronary vein versus right atrial or right ventricular blood, and the difference in pressure records obtained from these 2 sites.

BERNSTEIN

Bass, D. E., Kleeman, C. R., Quinn, M., Henschel, A., and Hegnauer, A. H.: Mechanisms of Acclimatization to Heat in Man. Medicine **34:** 323 (Sept.), 1955.

Intensive metabolic studies were performed on five healthy young soldiers who were acclimatized to heat by living and working in a temperature-controlled chamber. During control periods the temperature was kept at 76 F; the heat period lasted 14 days, with temperatures of 120 F. for the 12 daytime working hours, and 100 F. at night.

Successful acclimatization was achieved within the first week, during which time the sweat glands excreted more water relative to solutes. Evidence was obtained of an isotonic expansion of extracellular fluid, accompanied by renal retention of sodium and chloride in the first 4 days.

The authors propose the following explanation of the improved ability to work in the heat: On the first day the vascular bed enlarges due to cutaneous vasodilatation. With exercise, the disparity between blood volume and the vascular bed increases further, resulting in early signs of peripheral vascular collapse and decreased cardiac output. However, as blood and interstitial fluid volumes expand, cardiovascular responses improve and rectal temperature falls. After maximal expansion of the extracellular fluid occurs, no further improvement in work performance appears. The renal mechanism of salt retention in the first 4 days appears to be of great importance in the process of acclimatization. That acclimatization to heat is brought about by increased pituitary-adrenal activity was not supported.

ENSELBERG

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AHA SCIENTIFIC SESSIONS ABSTRACTS DUE BY JUNE 15

June 15 is the deadline date for submission of abstracts of papers intended for presentation at the 32nd Annual Meeting and 29th Scientific Sessions of the Association. This new deadline represents a postponement from the originally announced May 15 date. The Annual Meeting and Scientific Sessions are to be held in Cincinnati, October 26 to 31.

Under the present schedule, as tentatively established by the Program Committee of the Association's Scientific Council, the Scientific Sessions will get under way at the Cincinnati Music Hall on Friday evening, October 26, when a special program on instrumentation will be offered. This will include papers on electrocardiography, vectorcardiography, ballistocardiography, and in related fields.

The remainder of the scientific programs will be held on Saturday, Sunday and Monday, October 27 to 29. The mornings of these three days will be devoted to general scientific sessions, during which original papers of the widest professional interest will be presented, and to special lectures and a symposium. The lectures will be the George E. Brown and Lewis A. Conner Memorial Lectures. The symposium is planned in the field of cardiac rehabilitation.

The afternoons of Saturday, Sunday and Monday will be taken up with panels under the auspices of the Section on Clinical Cardiology, and with simultaneous specialized sessions of the other sections of the Scientific Council and of the Council on Rheumatic Fever and Congenital Heart Disease and the Council on Community Service and Education.

There will also be a special film program and both scientific and technical exhibits. Applications for scientific exhibit space must be submitted to the AHA by June 15. Those firms interested in presenting technical exhibits may obtain necessary information from Stephen K. Herlitz, 280 Madison Avenue, N. Y.

Abstracts of papers for presentation at the Scientific Sessions should be submitted in triplicate on special forms provided by the Association. They should not exceed 300 words in length. Information and forms may be obtained from the Medical Director, American Heart Association, 44 East 23 Street, New York 10, N. Y.

AHA FELLOWSHIP AWARDS TOTAL INCREASED TO 130

The Association has made 10 additional research fellowship awards for the fiscal year beginning July 1, 1956. This brings the adjusted total of such awards to 130 amounting to $825,000. The awards include 3 continued career investigatorships, 46 continued established investigatorships, 18 new established investigatorships, 31 continued or renewed research fellowships and 32 new research fellowships. Still to be announced are the grants-in-aid which will round out the national portion of the AHA-affiliate research support program.

The additional awards are as follows (a listing of the previously announced awards was contained in the March, 1956 issue of *Circulation*):

New Established Investigator

Havel, Richard J., mechanisms of lipid transport and relation of altered lipid transport to atherogenesis, University of California School of Medicine, San Francisco.

Renewal Research Fellowships

Boucot, Nancy G., clinical renal problems with eventual study of effects of pulmonary electrolyte problems on kidney, Peter Bent Brigham Hospital, Boston.

Corcoran, John W., biosynthesis of vitamin B-12, Columbia University College of Physicians and Surgeons, New York.

Dontas, Anastasius S., pathophysiology of prolonged altered cardiovascular homeostasis, University of Athens, Athens, Greece.

Gonzalez, I. Ernest, influence of steroid hormones on histochemistry of vascular bed and its response to injury, Oklahoma Medical Research Foundation, Oklahoma City.

Hactel, Donald B., myocardial metabolism studies by coronary venous catheterization in intact animals and man, City Hospital and Western Reserve University, Cleveland.

Heath, Edward C., mechanisms for pentose phosphate metabolism, Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md.

Kuida, Hiroshi, background in circulatory physiology; pressure-volume characteristics of the pulmonary bed, University of Minnesota Medical School, Minneapolis.

Lamfrom, Hildegard, fundamental techniques in protein and peptide chemistry, Carlsberg Laboratories, Copenhagen, Denmark.

von Kaulla, Kurt N., fibrinolytic enzymes, University of Colorado Medical Center, Denver.

AHA TO COOPERATE IN PROGRAM WITH RHEUMATISM ASSOCIATION

The Association's Council on Rheumatic Fever and Congenital Heart Disease will again cooperate in the presentation of a rheumatic fever program at the Annual Meeting of the American Rheumatism Association, which is to be held June 8 to 9 at the Conrad Hilton Hotel in Chicago. The AHA program, being prepared under the direction of the Council's Program Committee, of which Louis E. Martin, M.D., Los Angeles, is chairman, is scheduled tentatively for Saturday morning, June 9.

Persons interested in any aspect of the program of the Chicago meeting may obtain details from Edward F. Hartung, M.D., 580 Park Avenue, New York. Those who wish to reserve hotel space in Chicago should write to Edward F. Rosenberg, M.D., 109 North Wabash, Chicago 2.

AHA PROVIDES EDUCATIONAL MATERIALS FOR USAF PHYSICIANS

Two complete sets of Association professional educational materials have been turned over to the United States Air Force, one for the use of Air Force medical personnel stationed in Europe and another for USAF physicians in Japan.

The special units were prepared in accordance with an agreement between the Association and the Defense Department. This agreement lays the groundwork for widespread cooperation between the Association and the military in bringing the latest knowledge and techniques in cardiovascular education to the service physician.

The education units for overseas distribution each include the following:

Functional heart model, fluorodemonstrator with set of 12 normal and abnormal heart models, three Cardiac Clinic audiovisual kits, two Cardio-Views visual kits, tape library of heart sounds and murmurs, a number of recent professional publications of the Association, subscriptions to *Circulation* and *Circulation Research* and sufficient copies of *Modern Concepts of Cardiovascular Disease*, the Association's monthly bulletin for practitioners, for all USAF medical officers.

Additional cooperative plans for professional education have also been established by the Association with the other branches of the service.

AHA TO REVIEW ABSTRACTS FOR HAVANA CONGRESS

Research investigators in the United States who wish to present papers at the Fifth Inter-American Congress of Cardiology to be held in Havana, November 11 to 17, should submit abstracts of no more than 200 words to the American Heart Association, 44 East 23 Street, New York 10, no later than July 1. In accordance with the by-laws of the Inter-American Cardiologic Society, the papers will be reviewed by the Association and then transmitted to the Congress Committee.

MAY 31 ABSTRACTS DEADLINE FOR ARTERIOSCLEROSIS UNIT

May 31 is the deadline for submission of abstracts for anyone desiring to present a scientific paper at the annual meeting of the American Society for the Study of Arteriosclerosis. The meeting is to be held in Chicago, Novem-

ber 11 to 12. Factual abstracts should be submitted to Dr. R. Gordon Gould, P. O. Box 1663, Los Alamos, N. M.

PLAN 1957 RHEUMATIC DISEASES WORK CONGRESS IN TORONTO

The Ninth International Congress on Rheumatic Diseases has been scheduled for Toronto, June 23 to 28, 1956. The Congress, a quadriennial event, is expected to bring together physicians and research investigators from more than 40 nations. Additional information may be obtained from Richard T. Smith, M.D., 330 South 9th Street, Philadelphia 7.

CLINIC FOR CARDIAC SURGERY TO OPEN IN COLOMBIA

What is believed to be South America's first clinic for cardiac surgery is now under construction in Bogota, Colombia. It is scheduled to open in August of this year.

The clinic will start with a 15 bed surgical ward, an out-patient department, a catheterization unit, equipment for performing surgical procedures under hypothermia and special closed-circuit television apparatus to permit visiting physicians and students to witness operations.

The clinic's medical director will be Dr. Fernando Valencia-Cespedes who spent four years as a postgraduate student in the United States under Frank Wilson, M.D., at the University of Michigan and C. E. Kossman, M.D., at New York University.

PUBLISH ENGLISH-LANGUAGE GERMAN MEDICAL JOURNAL

Publication of an English-language German Medical Monthly has been inaugurated. The German journal will contain translations of articles appearing in the weekly *Deutsche Medizinische Wochenschrift*. Information and sample copies of this publication may be obtained from the Intercontinental Medical Book Corporation, 381 Fourth Avenue, New York 16, N. Y.

MEETINGS CALENDAR

June 7–10: American Therapeutic Society, Chicago. O. B. Hunter, Jr., 915 19 St. N.W., Washington, D. C.

June 7–10: American College of Chest Physicians, Chicago. Murray Kornfeld, 112 E. Chestnut St., Chicago 11.

June 9: North American Chapter, International Society, of Angiology, Chicago. Henry Haimovici, M.D., 105 E. 90th Street, New York 28.

June 10: Society for Vascular Surgery, Chicago. Henry Swan, M.D., 4200 East 9th Ave., Denver 7.

June 11–15: American Medical Association, Chicago. George F. Lull, 535 N. Dearborn St., Chicago 10.

June 18–20: American Neurological Association, Atlantic City. Charles Rupp, 133 South 36th St., Philadelphia 4.

July 23–26: International Congress of Developmental Biology, Providence, R. I. Prof. Paul Weiss, Rockefeller Institute for Medical Research, 66th St. and York Ave., New York 21.

ABROAD

June 14–15: Canadian Heart Association, Quebec City. John D. Keith, M.D., 555 University Ave., Toronto 2, Ontario.

July 22–27: 8th International Congress of Pediatrics, Copenhagen, Denmark. 8th International Congress of Pediatrics, Domus Medica, 12A Kristianiagade, Copenhagen, Denmark.

July 22–28: 8th International Congress of Radiology, Mexico City. Dr. Jose Noriega, Secretary General of Congress, Tepic 126 (2e piso), Mexico, D.F. 7.

July 30–Aug. 4: 20th International Physiological Congress, Brussels. Prof. J. J. Reuse, Faculté de Médicine et de Pharmacie, 115 Boulévard de Waterloo, Brussels.

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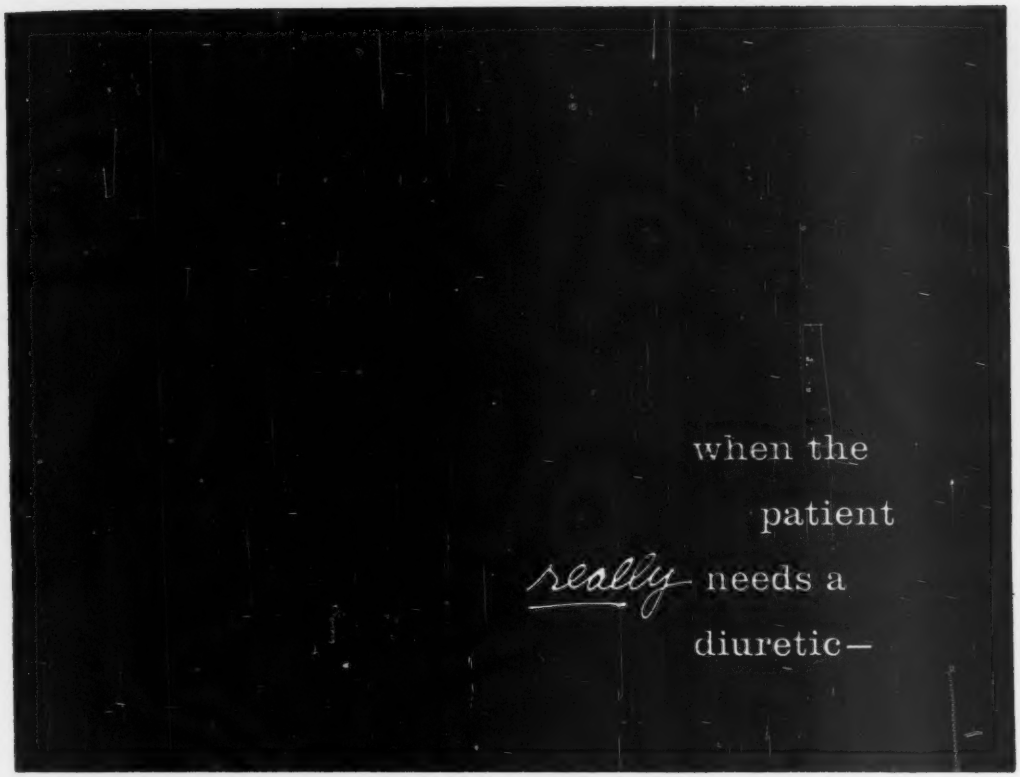

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